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SATURDAY OCTOBER 24 1953

TABLE OF CONTENTS

Changes in the Mean Stature and Weight of British Children over the Past Seventy Years E. M. B. CLEMENTS, M.B., B.S. 897

A Method for the Rapid Estimation of the Percentage Oxygen Saturation and Oxygen Content of Blood O. L. WADE, M.D., M.R.C.P., J. M. BISHOP, M.B., M.R.C.P., G. CUMMING, PH.D., B.SC., and K. W. DONALD, D.S.C., M.D., F.R.C.P. 902

Thrombophlebitis Migrans and Carcinoma of Body and Tail of Pancreas M. H. OELBAUM, M.D., B.SC., M.R.C.P., and SABINA J. STRICH, B.M., B.Ch. 907

Multiple Myelomatosis with Haematemesis and Melaena T. B. WILLIAMSON, M.D. 910

Intravenous Iron in Rheumatoid Arthritis: Possible Prognostic Factors M. R. JEFFREY, M.D., M.R.C.P. 912

Actinomycotic Pyaemia J. D. BLAINEY, M.D., M.R.C.P., and E. O. MORRIS, PH.D. 913

Action of Thiouracil and Thyroxine Administration on Adrenal Function J. CORVILAIN, M.D. 915

A Tuberculin Survey in Stoke-on-Trent J. S. MILLER, T.D., M.B., Ch.B. 917

A Case of Cor Triloculare Biatriatum with Survival to Adult Life D. R. BARRY, M.D., D.C.P., and D. H. ISAAC, M.D., M.R.C.P. 921

MEDICAL MEMORANDUM

Perforation of Tuberculous Ulcer of Small Intestine. KENNETH M. DOUGLAS, F.R.C.S.Ed. 922

BOOK REVIEWS 923

CLINICAL PATHOLOGY

Venepuncture. I. A. B. CATHIE, M.D., M.R.C.P. 930

GENERAL ARTICLES AND NEWS

Duke of Edinburgh: Honorary F.R.C.S. 932
THE NEW ACADEMIC YEAR 932
REPORTS OF SOCIETIES 933
JOHN RADCLIFFE 933
NOVA ET VETERA 934
MEDICO-LEGAL 945
MEDICAL NEWS 947
QUESTIONS AND COMMENTS 949

OBITUARY

Sir Ewen Maclean, M.D., F.R.C.P., F.R.C.O.G. 941
J. H. Badcock, F.R.C.S., F.D.S. 943
Archibald Malloch, M.D., F.R.C.P. 943
R. H. Burne, M.A., F.R.S. 944
Nest Kahan, M.B., D.P.M., D.C.H. 944

LEADING ARTICLES

Economical Prescribing 925
Heights and Weights of Schoolchildren 926
Enzymes and Their Activities 927

ANNOTATIONS

Clot Retention 928
Medresco Hearing-aids 929

CORRESPONDENCE

Clinical Pathology in General Practice. A. J. N. WARRACK, M.D. 935
Orthopaedic Care in Poliomyelitis. W. RITCHIE RUSSELL, F.R.C.P. 935
The Human Foot. CHARLES A. PRATT, M.C.S.P.; J. H. HANBY, F.Ch.S. 935
Alcohol-induced Pain in Hodgkin's Disease. L. REMOUCHAMPS, M.D.; D. CROWLEY, M.B. 936

SUPPLEMENT

Full Contents on First Page of Supplement
A Visit to New Zealand. IAN D. GRANT, M.B., Ch.B. 173
Encouragement of Private Practice 175
General Medical Services Committee 176
Correspondence 178

CORRESPONDENCE—*cont.*

Cancer and the Public. JOHN MCFARLAND, F.R.C.S.Ed. 936
Phenylbutazone. MICHAEL KELLY, M.D. 936
A.C.T.H. and Cortisone in the Schönlein-Henoch Syndrome. M. G. PHILPOTT, M.D. 937
Encouraging Drug-resistant Tuberculosis. A. OGG, M.D. 937
Peripheral Neuritis Following Tetraethylthiuram Disulphide Treatment. W. K. BARRY, M.B. 937
Infective Hepatitis in Doctors. W. J. C. HILL, M.B., and J. WEIR, M.B. 937
Post-gastrectomy Syndrome. A. WILFRID ADAMS, F.R.C.S. 938
Splenic Venography. H. FULD, M.D. 938
Tuberculosis Classification. MILOSH SEKULICH, M.D. 938
The Broken Acrylic Head. K. H. PRIDIE, F.R.C.S. 939
The General Practitioner and the Psychiatrist. G. L. RUSSELL, M.B. 939
Modified Leucotomy Operations. L. DAVIDSON, L.R.C.P.Ed. 939
An American Cottage Hospital. D. C. DRUITT, M.R.C.S. 940

Vital Statistics 945

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY OCTOBER 24 1953

CHANGES IN THE MEAN STATURE AND WEIGHT OF BRITISH CHILDREN OVER THE PAST SEVENTY YEARS

BY

E. M. B. CLEMENTS, M.B., B.S.

(From the Department of Anatomy, University of Birmingham)

The popular belief that modern men are taller than their forebears is largely based on such evidence as the small size of the armour worn in the Middle Ages. This belief has been questioned in recent years. For example, there is no clear evidence to show that the mean height of men in this island has altered over the past hundred years. On the other hand, it has been definitely established that in Great Britain adult stature is reached earlier now than it was 70 years ago. In years gone by men belonging to the wealthier classes attained their maximum height at an earlier age than did men of the poorer classes. Recent data for Scotland have shown that the difference in growth rate between the social classes has now been eliminated (Clements and Pickett, 1952). Thus, Scotsmen in the lower-income groups attain their maximum height at the same age as those in the upper-income group. It is likely that similar changes in the stature of men will have occurred throughout the rest of Great Britain. All this would seem to imply that our forefathers, living in harder conditions, continued growing for some years after they had assumed such adult responsibilities as soldiering. It would also seem that the quicker rate at which children mature to-day, and the elimination of differences in the rate of growth between social classes, reflect a general improvement in the living conditions and health of the whole population.

The present paper deals with records of the mean stature and weight of British children over the past 70 years. Data earlier than this are both meagre and selected, and refer mainly to children applying for permission to work in factories. Changes in factory legislation over the years would obviously affect the sampling of such children ; for example, many children who would have been regarded as useful labourers in earlier times were no longer passed as fit for work in the 1870s.

Data

Anthropometric data have been examined for each of the following five periods:

(1) The late nineteenth century : the data for this period are represented by the records of the British Association Anthropometric Survey of 1883.

(2) The early twentieth century: the data for this period are represented by the following records: (*a*) a survey of children living in Glasgow in 1905 (Elderton, 1914); (*b*) measurements of children from English urban areas (Tuxford and Glegg, 1911) ; (*c*) measurements of London children (Heron, 1910) ; and (*d*) measurements of Birmingham children (Auden, 1909).

(3) The period after the first world war : the data for this period are represented by measurements of Glasgow children in 1921 (Tully, 1924).

(4) The period before the second world war : the data for this period are represented by measurements of children living in the North-east Health Division of London in 1938 (Menzies, 1940).

(5) The period after the second world war : the data for this period are represented by measurements of children living in the North-east Health Division of London in 1947 (Daley, 1950), and of children living in Birmingham in 1947–8 (Clements and Pickett, to be published).

Most of the children measured in these surveys were town dwellers.

With regard to the use of data relating to London children, it is of interest to note that Daley (1950) found no statistically significant differences between London divisional and London county averages. We may therefore take it that the figures used for children living in North-east London are representative of children living in the whole of London.

The data which have been compared in this paper are reported in Tables I to IV. All the data have been standardized.

Standardization of Measurements

Before any conclusions are drawn some of the factors which may account for the differences between the measurements of successive surveys must be considered. The differences may be due wholly, or in part, to errors of random sampling, to systematic errors in technique, to factors operative in different geographical localities, or to socio-economic factors. The size of the error due to random sampling may be minimized by restricting comparisons to mean measurements of large samples of children. The second possible source of error is more difficult to minimize. The major trouble is due to systematic differences in the way the data were reported rather than to differences in the way the measurements were taken. Thus, whereas anthropometric techniques are unlikely to differ for measurements of stature and weight, a difference of six months' growth in the mean measurements may be introduced by the method of recording children's ages. In some cases age is taken to the nearest birthday and in others to the previous birthday. Sometimes, as in the recent surveys of London children, age is calculated from the year of birth. Systematic errors will also be introduced by different methods of rounding the measurements at the time of the examination. For instance, in some surveys stature is recorded to $\frac{1}{4}$ in., and in others to $\frac{1}{2}$ in., while weight is sometimes recorded to the nearest 0.1 kg. and sometimes to the nearest pound. The amount of clothing worn when measurements are made

is not constant. Occasionally measurements of nude subjects are reported, but more often the subjects wear indoor clothing, with or without footwear.

Social and Economic Background of the Children.—The mean stature and weight of children attending elementary schools vary according to the socio-economic background of the family (Healy, 1952).§ Comparisons have therefore been made wherever possible between children with similar backgrounds. This was done by using the social classification of the Registrar-General (1931). In this scheme "social class" is determined by the occupation followed by the father or head of the household, as coded in the Classification of Occupations of the Registrar-General. Class I comprises professional occupations; class II, intermediate; class III, skilled; class IV, semi-skilled; and class V, unskilled occupations.

Geographical Factors.—Tables I to IV show that contemporary data from different urban areas are all very similar. Thus there is little difference between the mean statures and weights of children of the same age measured in London (Heron, 1910), Glasgow (Elderton, 1914), Birmingham (Auden, 1909), and "urban areas of England" (Tuxford and Glegg, 1911). The mean measurements recorded in 1947 of Birmingham and London children are also very similar. These findings suggest that geographical factors are hardly likely to account for any differences which may exist between measurements of successive surveys.

Small but consistent changes in human stature and weight will appear as changes in the mean measurements when they are recorded at intervals. On the other hand, the foregoing considerations indicate that, unless anthropometric techniques are closely standardized, small differences between the same measurements may be entirely fortuitous.

To facilitate comparison, the following conventions have been employed in standardizing the data used in the present paper:

Age has been taken to the last birthday. The adjustments necessary to standardize the mean height and weight for age have been made by simple interpolation from the recorded data.

Stature is given in inches, as measured without shoes.

Weight is given in pounds, as measured in indoor clothing but without shoes. Some data contained estimates of the weight of footwear, and where necessary these have been used in making adjustments.

The social and economic backgrounds of the children have been classified under three headings. Data for children from social classes I and II (professional and intermediate) have been combined under a composite "upper-income group"; data for children from class III (skilled) have been placed under the heading "middle-income group," whilst the data for children from social classes IV and V (semi-skilled and unskilled) have been combined under the composite heading "lower-income group." The authors of many of the surveys used in this study state either the

TABLE I.—*Standardized Mean Statures of Boys Aged 5–13 Years From 1880 to 1947*

Age	Clements and Pickett (to be pubd)	Daley (1950)	Menzies (1940)	Tully (1924)	Tuxford and Glegg (Urban) (1911)	Auden (1909)	Heron (1910)	Elderton* (1914)	British Association (1883)
	1947	1947	1938	1921–2	1909–10	1908	About 1905	1905	About 1880
Heterogeneous									
5	43·5	43·3	42·9	40·9	40·4	41·1†	—	40·9	39·7†
6	46·0	45·5	45·1	42·8	42·3	43·3	—	42·8	41·9
7	48·0	47·6	47·3	44·7	45·0	44·7	—	44·7	44·6
8	50·1	49·6	49·3	46·2	46·9	—	47·1	46·8	46·5
9	52·0	51·5	51·3	47·6	48·7	—	49·1	48·5	48·9
10	53·9	53·3	53·1	49·9	50·8	—	51·0	50·3	50·7
11	55·6	55·2	54·9	51·6	52·6	53·1	52·6	51·9	52·7
12	57·6	57·2	56·6	52·7	54·7	55·0	54·4	53·8	53·7
13	59·5	59·3	58·4	54·7	56·1	57·1	56·2	55·4	55·8
Upper-income Group									
5	(45·0)			42·0		—	—	42·1	—
6	(46·7)			44·1		—	—	43·9	—
7	(50·9)			46·0		—	—	45·8	—
8	(49·8)			47·9		—	47·7	47·9	47·6‡
9	(51·3)			48·9		—	50·1	49·9	50·0
10	(54·9)			51·8		—	52·3	51·7	52·0
11	(56·4)			52·8		55·0	53·7	53·4	53·7
12	(57·1)			54·5		56·6	55·5	55·0	55·3
13	(60·4)			56·9		58·6	57·8	56·8	57·4
Middle-income Group									
5	43·5			40·8		41·1	—	41·2	39·7
6	45·9			42·8		43·3	—	43·0	41·9
7	48·0			44·5		44·7	—	45·1	44·6
8	50·3			46·7		—	47·4	47·1	46·5
9	52·1			48·2		—	49·6	49·0	48·9
10	54·1			49·8		—	51·6	50·7	50·7
11	55·6			51·8		53·1	53·0	52·5	52·7
12	57·8			52·7		55·0	54·7	54·2	53·7
13	59·4			53·9		57·1	56·5	56·1	55·8
Lower-income Group									
5	43·0			40·3		39·1	—	40·8	38·6
6	45·9			42·4		41·6	—	42·6	41·1
7	47·8			44·3		42·6	—	44·5	43·5
8	49·4			45·4		—	46·5	46·4	44·6
9	51·6			47·1		—	48·4	48·3	47·0
10	52·7			49·5		49·5	50·2	50·0	48·1
11	55·2			50·9		50·0	51·8	51·5	49·1
12	57·4			52·1		53·5	53·6	53·5	51·8
13	59·6			53·9		54·9	55·2	54·7	53·2

Parentheses indicate samples of fewer than 20.

* The measurements of Elderton (1914) have been taken as representative of those of the second period when computing the differences given in Table V. The measurements used in the sample from the lower-income group are the means of Elderton's Samples A and B.

† Data derived from the samples of children in the middle-income group are used for the heterogeneous group if no better data exist

‡ In the first period, the measurements of children in the upper, middle, and lower-income groups are the measurements recorded for social class 2, the town artisan, and the pooled industrial schools respectively in the British Association Survey, 1883.

§It should be pointed out that measurements of children in independent schools are not considered.

TABLE II.—*Standardized Mean Statures of Girls Aged 5–13 Years From 1880 to 1947*

Age	Clements and Pickett (to be pubd)	Daley (1950)	Menzies (1940)	Tully (1924)	Tuxford and Glegg (Urban) (1911)	Auden (1909)	Heron (1910)	Elderton* (1914)	British Association (1883)
	1947	1947	1938	1921–2	1909–10	1908	About 1905	1905	About 1880
Heterogeneous									
5	43·2	43·0	42·5	40·4	40·2	41·1†	—	40·8	39·8†
6	45·6	45·0	44·5	42·0	42·2	43·3	—	42·4	41·8
7	47·5	47·2	46·6	43·9	44·6	44·7	—	44·1	43·6
8	49·4	49·3	48·8	46·0	46·3	—	47·1	46·2	45·6
9	51·4	51·4	50·9	47·9	48·3	—	48·8	48·0	47·4
10	53·7	53·3	53·0	49·6	50·9	—	50·7	49·9	49·0
11	55·9	55·4	55·2	51·2	52·1	53·4	52·8	51·9	51·5
12	58·0	57·7	57·3	53·6	54·8	55·8	55·2	53·9	54·0
13	60·2	59·6	59·3	55·9	56·7	57·4	57·3	56·1	56·2
Upper-income Group									
5	(43·6)			41·5			—	41·8	(40·0)‡
6	(45·7)			43·2			—	43·7	(42·5)
7	(47·8)			46·0			—	45·6	44·4
8	(49·0)			47·0			47·8	47·5	(47·2)
9	(53·9)			49·5			50·0	49·5	49·9
10	(54·8)			51·0			51·7	51·3	51·4
11	—			52·3			53·6	53·1	53·3
12	(60·0)			55·3			55·8	55·3	55·7
13	(59·3)			57·8			58·1	57·6	58·5
Middle-income Group									
5	43·2			40·5		41·1	—	41·0	39·8
6	45·7			42·0		43·3	—	42·8	41·8
7	47·4			44·1		44·7	—	44·6	43·6
8	49·6			46·3		—	47·2	46·6	45·6
9	51·3			48·5		—	49·0	48·5	47·4
10	53·7			50·0		—	51·1	50·3	49·0
11	55·8			51·6		53·4	53·2	52·2	51·5
12	57·8			53·9		55·8	55·4	54·3	54·0
13	60·2			54·7		57·4	57·4	56·2	56·2
Lower-income Group									
5	43·0			39·9		39·1	—	40·6	39·2
6	44·9			41·1		41·6	—	41·1	41·2
7	47·8			43·3		42·6	—	44·2	42·4
8	49·1			45·5		—	47·2	46·1	44·7
9	51·5			47·1		—	48·6	47·9	46·4
10	53·4			48·9		48·7	50·1	49·8	47·7
11	56·3			50·5		50·7	52·2	51·7	51·5
12	57·9			53·0		54·2	54·6	53·8	51·2
13	60·2			55·2		55·9	56·6	55·6	53·0

Parentheses indicate samples of fewer than 20. For footnotes, see Table I.

character of the district represented by the sample or the usual occupation followed by the children's parents. This knowledge has enabled much of the data to be grouped into the three broad groups given above. Material which could not be classified has been termed "heterogeneous" and is reported in a separate section of the tables.

TABLE III.—*Standardized Mean Weights of Boys Aged 5–13 Years From 1880 to 1947*

Age	Clements and Pickett (to be pubd)	Daley (1950)	Menzies (1940)	Tully (1924)	Tuxford and Glegg (Urban) (1911)	Auden (1909)	Heron (1910)	Elderton* (1914)	British Association (1883)
	1947	1947	1938	1921–2	1909–10	1908	About 1905	1905	About 1880
Heterogeneous									
5	44·0	42·4	42·4	39·9	38·1	—	—	40·0	38·4†
6	48·7	47·2	47·2	44·0	42·5	—	—	43·5	42·1
7	53·6	52·2	52·1	47·5	46·3	—	—	47·5	48·2
8	59·1	59·6	57·2	50·9	50·3	—	48·9	51·5	51·8
9	63·7	62·7	62·7	55·4	54·5	—	53·8	56·5	55·8
10	70·3	68·4	68·5	60·6	60·0	—	58·3	61·0	61·5
11	75·0	75·0	72·7	65·0	65·0	65·8†	63·0	66·0	66·5
12	82·7	82·3	81·6	68·5	71·6	70·0	69·1	71·0	70·5
13	91·7	91·2	89·0	74·8	77·2	78·5	75·9	77·0	76·5
Upper-income Group									
5	(46·2)			40·7			—	41·6	—
6	(50·2)			44·3			—	44·9	—
7	(57·6)			48·1			—	48·9	—
8	(56·3)			52·3			50·6	53·7	53·0‡
9	(57·6)			55·6			56·1	58·8	59·8
10	(72·2)			64·1			60·6	63·7	62·7
11	(77·9)			67·8			65·6	68·6	65·5
12	(80·0)			73·1			71·8	73·8	70·7
13	(104·5)			80·5			81·6	80·0	77·6
Middle-income Group									
5	44·0			41·3		—	—	40·2	38·4
6	48·2			44·4		—	—	44·2	42·1
7	53·0			47·0		—	—	48·0	48·2
8	59·0			52·0		—	48·9	52·2	51·8
9	63·6			56·6		—	54·4	57·0	55·8
10	70·7			58·5		—	59·7	61·7	61·5
11	75·5			63·9		65·8	64·1	65·2	66·5
12	82·7			65·6		70·0	69·0	72·3	70·5
13	90·9			68·1		78·5	79·1	78·9	76·5
Lower-income Group									
5	44·2			38·5		—	—	39·8	34·2
6	48·4			43·7		—	—	43·2	37·9
7	53·9			47·6		—	—	46·9	43·2
8	58·3			49·7		—	48·9	50·9	44·6
9	62·7			54·8		—	53·1	55·4	49·9
10	67·5			61·0		58·1	57·0	59·9	54·3
11	72·4			64·3		57·0	62·1	64·6	60·7
12	82·7			67·8		65·1	67·2	69·7	64·9
13	90·4			74·6		73·0	72·2	74·4	69·8

Parentheses indicate samples of fewer than 20. For footnotes, see Table I.

TABLE IV.—*Standardized Mean Weights of Girls Aged 5–13 Years From 1880 to 1947*

Age	Clements and Pickett (to be pubd)	Daley (1950)	Menzies (1940)	Tully (1924)	Tuxford and Glegg (Urban) (1911)	Auden (1909)	Heron (1910)	Elderton* (1914)	British Association (1883)
	1947	1947	1938	1921–2	1909–10	1908	About 1905	1905	About 1880
Heterogeneous									
5	41·2	41·3	41·2	38·4	37·3	—	—	39·0	38·3†
6	44·8	45·5	45·8	42·1	40·6	—	—	42·0	41·1
7	49·6	50·5	50·7	45·0	45·0	—	—	46·0	44·2
8	54·0	56·1	56·2	49·4	48·9	—	48·2	49·5	49·8
9	59·3	61·5	61·9	53·9	54·2	—	52·7	54·0	53·2
10	67·0	67·9	68·1	57·4	58·6	—	57·8	58·5	58·5
11	76·5	76·3	75·7	61·2	64·4	65·6†	64·2	64·5	64·8
12	83·3	86·1	84·9	68·9	72·3	74·1	72·1	71·0	72·9
13	93·7	95·5	94·6	79·1	79·1	81·2	78·9	79·0	82·9
Upper-income Group									
5	(44·5)			39·2			—	39·9	(36·8)
6	(48·3)			42·8			—	43·7	(39·4)
7	(52·7)			46·4			—	47·5	43·4
8	(55·8)			50·1			48·3	51·8	(50·5)
9	(67·0)			55·0			55·1	56·6	53·0
10	(75·4)			59·8			59·9	61·6	60·9
11	—			64·1			66·3	67·4	66·5
12	(105·6)			74·0			74·3	74·6	75·3
13	(84·2)			—			82·4	83·9	86·2
Middle-income Group									
5	43·9			40·1		—	—	39·6	38·3
6	47·4			43·3		—	—	43·0	41·1
7	51·8			45·8		—	—	46·4	44·2
8	56·7			50·7		—	48·3	50·4	49·8
9	61·1			55·9		—	52·7	54·8	53·2
10	69·0			57·6		—	58·2	59·4	58·5
11	78·9			60·3		65·6	64·8	65·1	64·8
12	83·8			66·4		74·1	72·7	72·2	72·9
13	95·9			71·3		81·2	80·9	79·5	82·9
Lower-income Group									
5	43·4			37·0		—	—	38·6	35·0
6	45·2			41·3		—	—	41·8	38·7
7	52·7			44·3		—	—	44·3	42·1
8	55·8			48·5		—	48·9	49·1	45·8
9	63·3			52·4		—	52·9	53·2	50·8
10	67·0			56·4		52·6	57·3	57·7	54·0
11	78·0			60·7		57·9	62·0	63·1	59·0
12	85·8			68·6		69·3	70·8	69·7	66·3
13	96·6			78·9		76·3	77·4	76·2	70·8

Parentheses indicate samples of fewer than 20. For footnotes, see Table I.

Method of Measuring Differences

The method of estimating differences between measurements is the same for all social classes and for all periods from 1880 to 1947. A change in a measurement is determined by comparing the average measurement for each age-class at the beginning of a period with the corresponding

TABLE V.—*Changes in Mean Stature and Weight by Age and Income Group from 1880 to 1947*

Income Group	Period	Approximate Dates	Boys						Girls					
			Height in Inches			Weight in lb.			Height in Inches			Weight in lb.		
			5/7	8/10	11/13	5/7	8/10	11/13	5/7	8/10	11/13	5/7	8/10	11/13
Heterogeneous	Late 19th century	1880 to 1905	0·5	0·0	0·0	0·5	0·0	0·0	0·5	0·5	0·0	1·0	0·0	−2·0
	First world war	1905 ,, 1920	0·0	−0·5	−0·5	0·0	−0·5	−2·0	0·0	0·0	0·0	−0·5	−0·5	−1·5
	Inter-war years	1920 ,, 1940	2·0	3·0	3·5	3·5	7·0	12·0	2·0	3·0	3·5	4·0	8·5	15·0
	Second world war	1940 ,, 1947	0·0	0·0	0·5	0·0	0·5	1·5	0·5	0·5	0·0	0·0	0·0	1·0
	Total		2·5	2·5	3·5	4·0	7·0	11·5	3·0	4·0	3·5	4·5	8·0	12·5
Upper-income group	Late 19th century	1880 ,, 1905	—	0·0	0·0	—	0·0	2·5	1·5	0·0	−0·5	3·5	2·0	−0·5
	First world war	1905 ,, 1920	0·0	0·0	0·0	−0·5	−1·0	0·0	0·0	0·0	0·0	−1·0	−1·5	−0·5
	Inter-war years	1920 ,, 1940	3·5	2·5	3·0	7·0	4·5	13·5	2·0	3·5	3·0	5·5	11·0	—
	Second world war	1940 ,, 1947												
	Total		3·5*	2·5	3·0	6·5*	3·5	16·0	3·5	3·5	2·5	8·0	11·5	—
Middle-income group	Late 19th century	1880 ,, 1905	1·0	0·0	0·5	1·0	0·5	1·0	1·0	1·0	0·0	1·5	1·0	−1·0
	First world war	1905 ,, 1920	0·0	−0·5	−1·5	0·0	−1·0	−6·5	−0·5	0·0	−0·5	0·0	0·0	−6·0
	Inter-war years	1920 ,, 1940	3·0	4·0	5·0	4·0	8·5	17·0	3·0	3·0	4·5	4·5	7·5	20·0
	Second world war	1940 ,, 1947												
	Total		4·0	3·5	4·0	5·0	8·0	11·5	3·5	4·0	4·0	6·0	8·5	13·0
Lower-income group	Late 19th century	1880 ,, 1905	1·5	1·5	1·5	4·5	5·5	4·0	1·5	1·5	1·5	3·0	3·0	4·0
	First world war	1905 ,, 1920	0·0	−1·0	−1·0	0·0	0·0	−0·5	−1·0	−0·5	−0·5	−1·0	−1·0	0·0
	Inter-war years	1920 ,, 1940	3·0	4·0	5·0	5·5	7·5	13·0	3·5	4·0	5·0	6·0	9·5	17·5
	Second world war	1940 ,, 1947												
	Total		4·5	4·5	5·5	10·0	13·0	16·5	4·0	5·0	6·0	8·0	11·5	21·5

* No data for 1880–1905.

measurement at its end. To illustrate the procedure adopted, data will be considered for boys from the heterogeneous class. Examination of Table I will show that the differences between the mean measurements of 5-, 6-, and 7-year-old boys are similar. Consequently it was considered justifiable to regard these three age-classes as a single sample. The stature of this sample is represented by the average of the three measurements. In a similar way average figures have been calculated for the mean heights of the 8-, 9-, and 10-year-old boys and for the 11-, 12-, and 13-year-old boys. Thus it can be calculated from the figures given in Table I that the average stature for the 5 to 7 age-class of boys was 42.07 in. in 1880 and 42.8 in. in 1905. Hence the change in height of the boys of the 5 to 7 age-class between 1880 and 1905 was 0.73 in. The mean weight of boys is given in Table III, and the mean statures and weights of girls are given in Tables II and IV respectively. Changes in the weights of the boys and of the weights and heights of the girls have been determined by the method outlined above. The differences found between the measurements are given in Table V and shown in Charts 1 and 2.

Differences in the measurements of less than 0.5 in. or 0.5 lb. are regarded as unimportant and recorded as 0. Differences of one-half but less than one are recorded as 0.5 in. or lb., and so on. Thus the difference between the average heights of the samples of 5- to 7-year-old boys at 1880 and 1905 was 0.73 in. This figure is recorded as 0.5 in.

The use of the word "children" in the text implies both boys and girls; otherwise the sex is specified. When measurements in Table V are similar for boys and girls of the same age-class, the average of the two measurements is given in the text and referred to as "measurements of children."

Results

Data given in Tables I to IV indicate that children are growing more quickly now than they were some years ago. Comparison of the figures given by Heron (1910) and Daley (1950) serves to illustrate this trend. In both surveys measurements were recorded of children living in London. Possible variations due to sampling in different geographical localities are thus minimized. It will be apparent that average children living in 1947 are 2 in. taller and 8 lb. heavier than children of the corresponding age and income group living in 1910. Furthermore, the more recent data show that children of the heterogeneous group are taller and heavier than children in the upper-income group living in 1910.

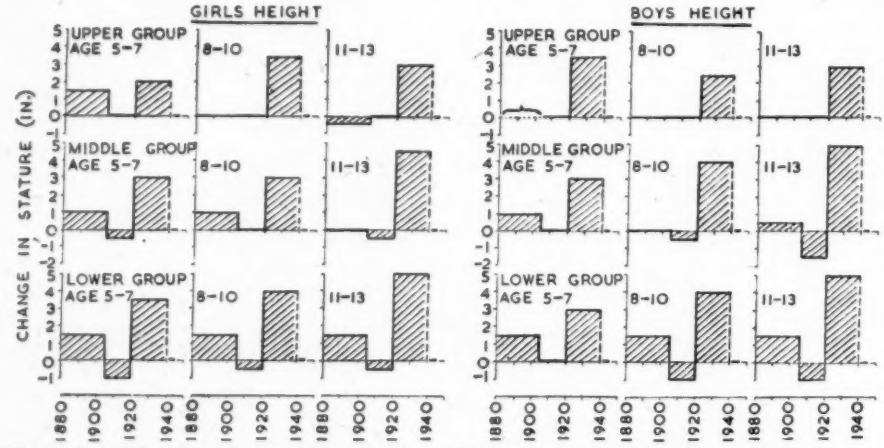

CHART 1.—Changes in mean stature, by age and income group, from 1880 to 1947. Changes found in the years from 1920 to 1947 (period of the inter-war years and the second world war) have been attributed to the years from 1920 to 1940. This is indicated by a coarse broken line terminating the period in 1940. For explanation see text. A finely broken bracketed base line indicates no data.

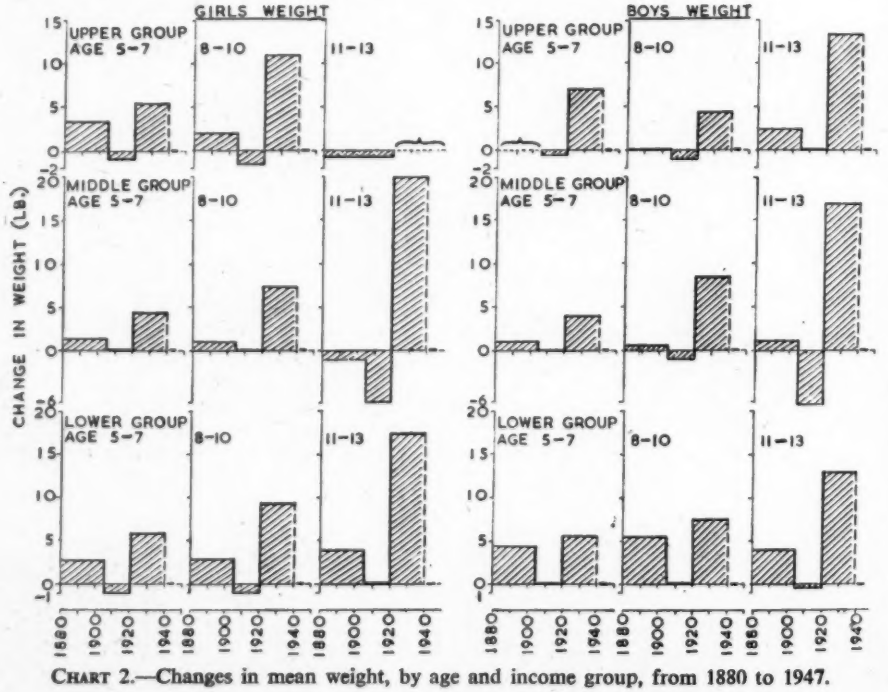

CHART 2.—Changes in mean weight, by age and income group, from 1880 to 1947.

The broad outline of the changes in each period will be evident on consideration of the data for the heterogeneous income groups given in Table V. The sample of 5-, 6-, and 7-year-old children measured in 1947 was 2.5 in. taller and 4 lb. heavier on the average than the sample measured in 1883. Children aged 8, 9, and 10 years were about 3 in. taller and 7 lb. heavier, and those aged 11, 12, and 13 years were 3.5 in. taller and 9 lb. heavier.

Similar trends are found when data for the three income groups are examined in detail. In addition, however, several subtle variations in the findings become apparent when the groups are compared one with another. Thus, over the seventy-year period the increases in average stature and weight of children in the lower-income group were greater than those in the corresponding samples of children in the upper-income group. Average children in the lower group aged 5 to 7 years increased in stature and weight by 4 in. and 9 lb., those aged 8 to 10 years by 4.5 in. and 12 lb., and those aged 11 to 13 years by 5.5 in. and 19 lb.

Period of the Late Nineteenth Century.—It will be seen from the samples of the heterogeneous income groups that at the beginning of the twentieth century average girls of the age-classes 5 to 7 and 8 to 11 were both 0.5 in. taller than their earlier counterparts. The 5- to 7-year-olds were also 1 lb. heavier. The sample of boys aged 5, 6, and 7 years measured in 1905 were 0.5 in. taller and 0.5 lb. heavier on the average than the corresponding sample measured in 1883. Children in every age-class of the lower-income group were, on the average, about 1.5 in. taller and 4 lb. heavier at the end of this period than they were at the

beginning. Increases in the mean stature and weight of children in the upper- and middle-income groups were generally smaller and less consistent, and were usually confined to the youngest samples of children. In the upper-income group, for example, only the sample of girls aged 5 to 7 years showed an increase in height, amounting to 1.5 in. Girls aged 11 to 13 years in the upper-income group were 0.5 in. shorter and weighed 0.5 lb. less at the end of the period than at the beginning.

Period of the First World War.—During the period from 1905 to 1921 there were no increases in average height of comparable samples in the heterogeneous income group. Two samples of boys, aged 8 to 10 and 11 to 13 years, were actually 0.5 in. shorter on the average at the end of the period than they were at the beginning. The average stature of children in every age-class of the upper-income group was unchanged during this period. On the other hand, the average statures of 9 out of 12 samples of children in the middle- and lower-income groups were from 0.5 to 1.5 in. shorter in 1921 than similar samples of children measured in the same city (Glasgow) in 1905. Changes in the average weight of children during this period were less consistent. The average weights of all except one sample in the heterogeneous group were decreased. The exception was the 5- to 7-year-old boys, who showed no change in weight. The greatest change, a reduction of about 6.5 lb., was recorded in 11-, 12-, and 13-year-old children of the middle-income group.

Period of the Inter-war Years, and of the Second World War.—In the inter-war years considerable increases in average stature and weight occurred in every age-class of the heterogeneous income group. Children aged from 5 to 7 years were, on the average, 2 in. taller and 3.5 lb. heavier, those aged 8 to 10 were 3 in. taller and 7 lb. heavier, and those aged 11 to 13 were 3.5 in. taller and 12 lb. heavier at the end of the period than at the beginning. In several instances the increases recorded in this period of about twenty years were greater than the total increase over the seventy-year period, because earlier losses were being made up.

The rapid rate of increase in average stature and weight stopped at the start of the second world war. A comparison of the samples measured in 1938 and 1947 shows small increases of 0.5 in. in mean stature in three out of the six groups. In three of the four groups of children aged 8 to 13 years there were increases in mean weight of up to 1.5 lb.

The period covered by the samples of the separate income groups extends from 1921 to 1947 and includes the second world war. Judging from the evidence of the heterogeneous samples from 1938 to 1947, however, it is likely that the major changes in all income groups occurred before 1938. Children of all age-classes were taller and heavier in 1938 than were corresponding samples in 1921. In the lower-income group the average stature and weight of children aged 5 to 7 years were 3 in. and 5.5 lb. more, those of children aged 8 to 10 years were 4 in. and 8.5 lb. more, and those of children aged 11 to 13 years were 5 in. and 15 lb. more at the end of the period than at its beginning. The average stature of 9 out of 12 samples of children in the middle- and lower-income groups increased by at least 0.5 in. more than that of children in the upper-income group. However, children of the lower-income group show no consistently greater increase in weight.

Discussion

In 1876 Roberts made the observation that "a factory child of the present day at the age of 9 years weighs as much as one of 10 did in 1833 . . . each age has gained one year in 40 years." The tendency noticed by Roberts for children to grow more quickly over a period of time has been continued to the present day. There can be no doubt that there have been great increases in the mean stature and weight of children since 1880. The extent of these increases, which have been described above, indicates an advancement in development of about eighteen months' growth. Thus the average 6-year-old child now has about the same height and weight as an average 7.5-year-old child of 1880: an average child of 12 years of age is about 3.5 in. taller than one of the same age 70 years ago. The change is even greater in the children in the lower-income group, and, on the average, is equivalent to two years' growth.

Contrary to a view expressed by Menzies (1940), a detailed examination of the data indicates that the rate of increase of growth has not been constant over the years. The increase, which was slow at first, ceased during the period of the first world war: indeed, actual losses of both weight and height occurred in many groups. During the following inter-war years, children of all income groups and age-classes increased rapidly in weight and height. This rate of increase was greatly retarded during the period which included the second world war.

In the period of the late nineteenth century the height of all samples of children in the lower-income group increased by 1.5 in. On the other hand, children of the upper- and middle-income groups showed no uniform increase in size. Thus increases of 1 in. or more were restricted to children aged 5, 6, and 7 years of those groups (no data for boys in the upper-income group), and to girls aged 8 to 10 years in the middle group. Two explanations of these increases are considered. One is that some environmental factors have a selective effect upon the younger children in the upper- and middle-income groups, and on children between 5 and 13 years of age in the lower-income group. The second explanation is that these groups of children respond in a sensitive way to slight changes in environment. During the first world war living conditions became more difficult when, for example, there were restrictions on the amount and quality of various foods that could be purchased. In that period the stature of each sample of children in the upper-income group remained unaltered, whilst the mean stature was decreased in four out of the six age-classes of children in the middle-income group, and in five out of the six similar classes in the lower-income group. These facts suggest that the second explanation is the more likely one.

The largest increases in mean heights and weights are found in children of the lower-income group. The difference between the increases in the mean statures of this group and those of the upper-income group is a matter of about 1 in. in the youngest children, 2 in. in children aged 8 to 10 years, and 3 in. in children aged 11 to 13 years. The increases in the mean weights are less consistent, but amount to about 2 lb. at 5 to 7 years, 5 lb. at 8 to 10 years, and (say) 7 lb. or more at 11 to 13 years. The differences existing between the mean statures and weights of children have been reduced by these changes. To-day, average children of the same age in the middle- and lower-income groups are the same height, whilst the average child in the upper-income group is about 2 in. taller. A similar relation holds true for the weight of girls. The average girls in the upper-income group are 2 lb. heavier than girls of comparable age in the middle- and lower-income groups, between whom there are no weight differences. Furthermore, weight differences between comparably aged boys of the three income groups have now been eliminated.

The findings described above differ greatly from those of seventy years ago. At that time average children in the upper-income group were 2 in. taller and 2 lb. heavier than children in the middle-income group, and the latter children were 2 in. taller and 5 lb. heavier than average children of the same age in the lower-income group.

In 1941 the mean stature of men in the upper-income group was 1.41 ± 0.15 in. more than that of men in the lower-income group (Clements and Pickett, 1952). This fact may indicate the interplay of genetic factors (Dahlberg, 1947), and implies that even when children in all income groups are growing at their optimum rate the mean stature of children of the same age in the different groups will differ from one group to another.

It is certain that similar changes have been taking place in other countries during the period under examination. For instance, in Toronto, Canada, typical 6-year-old elementary-school children were 2 in. taller in 1939 than in 1892, 9-year-old children were 3 in. taller, and 13-year-old girls and 14-year-old boys were about 3.2 in. taller. Half of the observed differences have taken place since 1923 (Meredith and Meredith, 1944).

It is clear that the remarkable changes which have occurred in the mean statures and weights of children over the last seventy years are part of a long-term trend in the growth of children. The changes defined not only imply the need of up-to-date height and weight standards for paediatric practice, and the making of corresponding adjustments in the size and relative dimensions of children's clothing and school equipment, but they make it apparent that anthropometric measurements can yield information of great interest.

Summary

Anthropometric measurements of children aged from 5 to 13 years, made between 1880 and 1947, have been standardized and examined.

The average stature and weight have increased by from 2.5 to 3.5 in. and from 4 to 11 lb. respectively over this period, the increases being greatest in the older children.

The increases found are greater than can be accounted for by systematic and random sampling errors, and indicate that, on the average, there has been an acceleration of 18 months' growth. Thus an average 6-year-old child is now of much the same size as one of 7.5 years in 1880.

The rate of increase in mean stature and weight is not constant over the years. It begins slowly, and is first evident in the lower-income group and in the 5- to 7-year-old children in the upper- and middle-income groups. The rate of increase was greatest in the inter-war years, when it was shown by all groups. The upward trend was interrupted during both the first and the second world wars. The increase in the mean measurements has been greatest in the lower-income group, so that the difference which existed in 1880 between the average measurements of children in this group and the middle-income group no longer exists. The differences in stature and weight between average children in the upper- and lower-income groups were 4 in. and 7 lb. in the late nineteenth century and 2 in. and 2 lb. in 1947.

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A METHOD FOR THE RAPID ESTIMATION OF THE PERCENTAGE OXYGEN SATURATION AND OXYGEN CONTENT OF BLOOD

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The manometric method of Van Slyke and Neill (1924) is the standard procedure for the estimation of blood oxygen content and capacity. This manometric analysis is time-consuming and makes heavy demands on laboratory workers. Further, since the reliability of results diminishes with fatigue, the number of blood samples that can be accurately analysed on any single occasion is limited. In this paper a spectrophotometric method of estimating the percentage oxygen saturation, the oxygen capacity, and the oxygen content of blood is described. It employs relatively simple apparatus, allows the rapid analysis of a large number of blood samples, and has been found most valuable in the study of the cardiac output and the investigation of abnormal shunts in the heart and great vessels.

Photometric methods of estimating the haemoglobin content and oxygen saturation of blood have been in use in laboratories for some 20 years; Hall (1934) and various German workers, notably Kramer (1934), described methods which were not, however, suitable for routine use in clinical investigations.

In 1936 Drabkin and Austin described a new type of spectroscopic cell or cuvette of 0.007 cm. depth which enabled them to study haemolysed undiluted blood under anaerobic conditions. Valuable fundamental information was obtained, but the method was not suited to routine estimations on multiple samples. Most of the subsequent methods are based on the data obtained by these workers, who showed that Beer's law (see below) was valid for haemoglobin solutions. These workers (Drabkin and Austin, 1936; Hickham and Frayser, 1949; Nahas, 1951) employ cuvettes and precision spectrophotometers of the Beckman type, and readings are taken at two wave-lengths to increase accuracy.

The method here described is a modification of that devised by Gatman (1952).

Principle of the Method

The method is based on the measurement of the optical density of haemoglobin solutions. The optical density D of any medium is defined by Lambert's law as follows:

$$D = \log_{10} \frac{Io}{I}$$

where Io is the intensity of the incident light and I the intensity after transmission by the medium considered.

The optical density of any medium depends on the length of the light pathway through that medium and upon its absorption characteristics—i.e. :

$$D = E\,d$$

where d is the path-length and E is the extinction coefficient, which is constant for a given medium, wave-length, and wave-band width.

Beer studied the optical properties of solutions, and showed that the optical density of a light-absorbing solution was directly proportional to its concentration. In dealing with solutions, therefore, Lambert's law is modified as follows :

$$D = E.c.d$$

where c is the concentration of the solution. Thus the concentration of a single pigment can be easily measured by determination of the optical density of the solution.

The determination of percentage saturation of haemoglobin, however, involves the measurement of the relative concentration of two separate pigments (haemoglobin and oxyhaemoglobin) each with its own characteristic extinction coefficient. The optical density of a solution of blood will be a function of the relative amounts of the two pigments present. If the optical density of aliquots of the same solution in the same tube is determined, in which all pigment has been respectively reduced and oxygenated, then the percentage saturation is easily obtained from the following proportionality equation,

$$\text{Percentage saturation} = \frac{D_{Hb} - D_{mixed}}{D_{Hb} - D_{HbO_2}}$$

Thus the three measurements necessary for the determination are as follows : (1) the optical density of the original anaerobic blood solution, D mixed ; (2) the optical density of the blood solution reduced, D_{Hb} ; (3) the optical density of the blood solution oxygenated, D_{HbO_2}

It will be noted that, under the constant conditions specified, the optical properties of the tube need not be considered in the determination of percentage saturation.

The optical densities are measured with light of a wave-length of 630 mμ. The absorption curves for haemoglobin and reduced haemoglobin show that the rate of change of optical density with wave-length is small in this region. This minimizes any error caused by slight changes in the calibration of the spectrophotometer.

Measurements of total haemoglobin content, and thus of the oxygen capacity of blood, are made at a wave-length of 540 mμ ; for here, with a wave-band of about 30 mμ as used in this method, the optical densities of haemoglobin and reduced haemoglobin are equal. If a known constant dilution of blood is made and the optical density is measured, the haemoglobin content may be found from the linear relationship obtained by previous direct calibration against estimations of oxygen capacity made by the Van Slyke and Neill method.

Most of the optical methods to determine the percentage saturation of blood *in vitro* described previously require the Beckman spectrophotometer, a precision instrument which is not often available in clinical laboratories. In the method here described an instrument which is found in most biochemical laboratories is used, and satisfactory results are obtained with considerably diluted blood solutions. This allows the use of sample tubes made of inexpensive glass tubing with a relatively long light path, and obviates the need for special cuvettes, which are in any case unsuited for rapid estimations on large numbers of blood samples.

Details of the Method

The following apparatus and solutions are required :

1. A unicam spectrophotometer (model S.P. 350), which is modified by inserting a half-inch-square mask on the light condenser and by narrowing the collimator slit. This reduces the wave-band width to about 30–40 mμ, but there is some sacrifice of light intensity. It is thought probable that satisfactory results would be obtained on the unmodified instrument, but this has not yet been demonstrated. A holder for tubes of 8 mm. diameter, on which an alignment mark is engraved, replaces the usual holder. The spectrophotometer is switched on half an hour before readings are taken. It is advisable to check the wave-length calibration on each occasion with a carefully cleaned didymium glass filter.

2. Sample tubes for the spectrophotometer. These are made from heat-resisting glass tubing of 6 mm. bore and 8 mm. external diameter. The use of special optical glass or precision tubing is unnecessary. Each tube is 11 cm. long, is numbered, and has a longitudinal line inscribed on its upper end with a diamond. Alignment of the line with the mark on the spectrophotometer holder ensures that an identical optical pathway is used each time a reading is taken with a given tube. After each experiment the tubes are washed with tap water, rinsed with distilled water, and dried by heat.

3. Boiling-tubes ½ in. (1.25 cm.) diameter by 4½ in. (11.4 cm.). These are numbered and provided with lips to facilitate pouring.

4. Numbered racks to hold 30 sample tubes and 15 boiling-tubes.

5. Angled needles used for diluting and handling the blood. These are made from steel tubing 1 mm. bore and 13 cm. long soldered to a needle hub. In each needle there is a right-angle bend 1 cm. from the needle hub. It is important that the needle tip should reach the bottom both of the sample tubes and the flask containing the diluting solution.

6. Gas-free solution of sodium carbonate and saponin, which is prepared freshly for each experiment. Two hundred ml. of 0.1% sodium carbonate solution is boiled for 15–20 minutes in a conical flask, allowance for evaporation being made by the previous addition of distilled water to the solution. Immediately after boiling, a few millilitres of the solution are decanted to dissolve 1 g. of pure white saponin. When the saponin* has dissolved, the resulting solution is poured back down the side of the conical flask into the boiled solution. A layer of liquid paraffin is poured over the surface of the solution, which is then allowed to cool. It must not be shaken, and can be used during the next 24 hours. It is convenient to keep the flask tilted in a small wooden holder.

7. Cold saturated sodium hydrosulphite solution, which is made up freshly for each day's work.

8. Sample tubes, 1 cm. by 9 cm., as supplied with the spectrophotometer, for the estimation of blood oxygen capacity.

Estimation of Percentage Oxygen Saturation of Blood

Blood samples of 4 ml. are drawn into lightly oiled 10-ml. all-glass syringes, the dead space of which is filled with heparin or dextran sulphate (5,000 units per ml.). At the earliest possible moment after sampling, ½–¾ ml. of mercury is drawn into the syringe, which is sealed with a hub cap and vigorously shaken to ensure even distribution of the anticoagulant. While awaiting analysis the syringe is placed on a rotating cone so that sedimentation of red cells does not occur. For analysis the syringe hub is removed and an angled needle is fitted firmly to the syringe. Blood is expelled through the needle until the appropriate amount is left in the syringe, allowance being made for the mercury present. The carbonate–saponin solution is

*Pure white saponin is difficult to obtain, and the usual pigmented commercial material has not proved satisfactory. Preliminary experiments show that 0.5 ml. of a concentrated solution of the synthetic detergent "lissapol" can be used as a satisfactory substitute for the saponin. When lissapol is added to boiled distilled water the mixture becomes turbid, but the turbidity disappears on cooling.

then drawn into the syringe, care being taken to avoid drawing up globules of paraffin. The extent of dilution, which need not be of great accuracy, is as follows :

Haemoglobin Content of Blood, g. 100 ml. (Approx.)	Oxygen Capacity of Blood, Vols. % Oxygen (Approx.)	Ml. of Blood Diluted with Carbonate–Saponin Solution to 10 ml.
7·5	10	3
11	15	2·5
15	20	2
19	25	1·5
22·5	30	1

After dilution and shaking, the angled needle is detached and the syringe laid on the bench for at least five minutes to allow haemolysis of the blood, fifteen syringes of blood being treated in this manner at a time. When haemolysis is complete a clean angled needle is attached to each syringe. A few drops of the clear haemolysed solution are expelled through the needle and discarded, the tip of the needle is inserted to the bottom of a sampling tube, and 2.5 ml. of the solution is slowly injected, the needle tip being withdrawn as this is done so that it lies always just below the surface, undue turbulence being thereby avoided. The upper fluid acts as an efficient barrier, preventing oxygenation of the solution in the lower half of the tube, through which light is transmitted. It is not necessary to cover the surface with paraffin. Two tubes are filled from each syringe, and the remaining solution is transferred to a lipped boiling-tube to await oxygenation by the passage of a stream of oxygen bubbles for a period of half a minute.

When a rack of tubes has been filled the optical density of the "mixed solutions" is determined with reasonable dispatch. Before any series of readings the galvanometer is adjusted to indicate zero transmission with no light incident on the photocell, and then the intensity of light is adjusted to give 100% transmission (zero optical density) when there is no tube in the holder. The latter reading is adjusted, if necessary, each time a tube is withdrawn from the holder. Each sample tube is polished with a dry cloth and is placed in the holder and rotated until its engraved line is in alignment with the mark on the holder before the reading is taken on the logarithmic scale. It is convenient to take the "mixed" readings of all the tubes in the rack and then to reduce all the solutions. The contents of each tube are drawn into a Pasteur pipette which already contains about 0.1 ml. of the saturated solution of sodium hydrosulphite. The mixture is drawn up and down several times to effect complete mixing and to allow complete reduction of the haemoglobin, the most efficient method being to suck solution from the bottom of the tube and then pour it back on to the top of any remaining solution. Although care must be taken not to carry solution from one tube to another, there is no need to clean the pipette between each reduction. Each sample tube is again polished and placed in the holder in correct alignment and the optical density of the reduced solution is then read on the logarithmic scale. The reduced solution is now sucked out and discarded and the tubes are cleaned and dried with pledgets of cotton-wool on a burred metal rod. A small rat-tail file is useful. When the tubes are clean the oxygenated haemolysed solution is transferred to them from the corresponding boiling-tubes.

Most of these procedures are carried out with the tubes in the rack, as this reduces the amount of handling and the need for polishing. The optical densities of the oxygenated solutions are then read on the logarithmic scale.

From these three readings the percentage oxygen saturation is estimated and the mean of the results from each pair of tubes is taken, these results seldom differing by more than 1%. Two observers can, by this method, make duplicate estimations of the percentage oxygen saturation of 15 specimens of blood in one hour.

Occasionally small blood clots appear in the syringes despite the presence of the anticoagulants. This is often due to failure or delay in shaking the syringe after the addition of the mercury. If the syringe is held with the nozzle elevated for a short time the clots fall to the bottom and the tubes can be filled with solution which is free from clots. In this way accurate results can be obtained despite considerable clotting.

If good results are to be obtained cleanliness of apparatus and careful handling of the blood and the haemolysed solutions are essential. The commonest error is for air bubbles to be drawn into the syringe either when the blood is sampled or when the blood is diluted with the carbonate–saponin solution, the latter causing more serious errors.

The method used by Gatman (1952) differs in two respects from the method described here. In his method readings are taken with the reduced and oxygenated specimens of each blood sample in a pair of tubes that have to be optically matched. In the present method all readings are taken in the same tube. Secondly, reduction of the solution is effected by the addition of powdered sodium hydrosulphite, which in our hands occasionally causes precipitation and coagulation of blood proteins.

Determination of the Oxygen Capacity of Blood

This determination is necessary in order to convert percentage saturation into oxygen content. The capacity can be determined by any of the recognized methods; the one we have used is as follows. Light of wave-length 540 mμ is used. Four ml. of 0.1% sodium carbonate is pipetted into a standard tube of 1 cm. diameter, which is placed in its holder in the spectrophotometer. Twenty c.mm. of blood is next drawn up into a pipette and, with the tube in place, the light intensity is adjusted to give a reading of zero optical density so that the tube containing carbonate solution acts as its own blank. The tube is now withdrawn and the blood is added, the micropipette being rinsed in the usual manner to ensure complete delivery. After mixing, the tube is returned to the holder and the optical density is determined on the logarithmic scale. If the previously prepared haemoglobin solution is transferred to a 1-cm. cell for the reading to be taken, a second cell containing sodium carbonate solution may act as a blank. This method is just as convenient, and probably

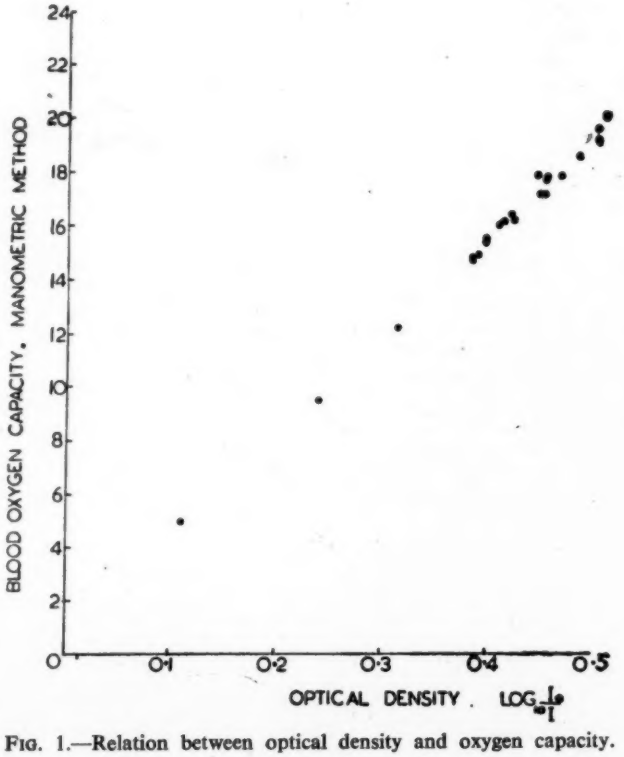

FIG. 1.—Relation between optical density and oxygen capacity.

gives more accurate results. It has been customary to take the mean of the readings of optical density of three dilutions provided the scatter between the greatest and smallest does not exceed 0.010. The haemoglobin content or oxygen capacity is then obtained from the calibration chart.

TABLE I.—*Relation Between Optical Density and Oxygen Capacity*

Optical Density $(\log \frac{I_0}{I})$	Blood Oxygen Capacity vols. % (Manometric Method)
0·313	12·32
0·499	19·64
0·483	18·66
0·409	16·10
0·398	15·75
0·238	9·47
0·444	17·94
0·418	16·51
0·453	17·86
0·537	20·63
0·383	14·87
0·506	20·10
0·398	15·49
0·421	16·28
0·602	23·17
0·523	20·13
0·466	17·93
0·111	4·50
0·446	17·33
0·383	14·80
0·452	17·32
0·412	16·21
0·451	17·80
0·390	15·01
0·500	19·23

Table I and Fig. 1 show the data with which the spectrophotometer was calibrated. Measurements of oxygen capacity were determined by the standard Van Slyke manometric method. The blood specimens had been rotated in a tonometer for twenty minutes in equilibrium with air. Although the coefficient of linear correlation between the spectrophotometer readings and the Van Slyke determinations is very high (0.99), it became apparent during the work which is here reported that a spectrophotometer in which the wave-length of light is adjustable is not the ideal instrument for the determination of absolute optical density, as the calibration of the instrument tends to vary slightly from day to day. The fault is of little importance in measuring the percentage saturation of blood where the result depends on the relationship of three consecutive readings taken within a short time of each other, and where the slight changes in the wave-length of the light from day to day would in any case have an insignificant effect on the results.

Comparison of Results Obtained by Spectrophotometric and Standard Manometric Analyses

1. The Oxygen Content of Blood Samples

An experiment was planned in which three consecutive samples of blood were collected within a period of a minute and a half from either an arterial needle inserted in a brachial artery or from a cardiac catheter with its tip lying in the pulmonary artery. The percentage oxygen saturation of the first and third samples was determined by spectrophotometry. The total haemoglobin content and oxygen capacity of one of the specimens was also determined spectrophotometrically, and two measurements of the oxygen content of blood were thus obtained. The second blood sample was submitted to two analyses of oxygen content by the Van Slyke and Neill standard manometric method. On 48 occasions samples of blood were obtained in which the two spectrophotometric estimates checked to within 0.2 vol. % oxygen content and in which the two estimates made by the manometric method checked with each other to within 0.2 vol. %. As it was felt that for the purposes of comparison the estimation by each method should be reliable, the results were rejected in all instances when the duplicate oxygen content estimations by either method differed by more than 0.2 vol. %.

TABLE II.—*Comparison of Measurements of Blood Oxygen Content (48 Observations on 15 Subjects)*

Subject	No. of Blood Samples	Oxygen Content in vols. %	
		Spectrophotometric	Manometric
A.118	1	12·76	13·39
	2	18·20	18·50
A.119	1	18·33	18·27
	2	18·85	18·66
A.120	1	17·78	17·65
	2	13·72	13·19
	3	17·84	17·31
	4	13·61	12·63
A.121	3	11·90	11·03
	4	18·06	17·10
	5	12·03	11·19
A.122	2	14·59	14·73
	3	11·31	11·21
	4	14·69	14·77
	5	11·14	10·87
A.123	1	15·29	15·73
	2	15·34	15·57
	3	16·35	16·90
A.124	2	15·36	15·25
	4	15·58	15·28
A.125	1	13·50	12·01
	2	17·42	16·42
	3	13·27	12·23
	4	17·53	16·21
A.126	2	16·96	16·52
	3	13·44	12·88
A.127	3	11·17	11·23
	4	18·66	18·33
A.128	1	14·55	13·96
	2	22·01	20·95
	3	14·48	13·82
	4	22·08	20·84
A.130	1	13·04	12·98
	2	19·00	19·12
	3	12·94	12·51
	4	19·10	18·89
A.132	1	14·53	14·24
	2	20·15	19·64
	3	14·61	13·72
	4	19·98	19·11
A.133	1	9·59	9·37
	2	15·84	15·78
	3	9·55	9·25
	4	15·99	15·95
A.134	1	14·71	14·45
	2	19·28	19·34
	3	13·65	13·69
	4	19·44	19·66

In Table II the mean of the duplicate estimates of oxygen content made by spectrophotometry is compared with the mean of the duplicate estimates made by the manometric method on the blood samples obtained on these 48 occasions. The results are plotted in Fig. 2.

There is a close relationship between the results obtained by the two methods, and the coefficient of linear correlation is $r=0.99$. More detailed analysis, however, reveals signs of heterogeneity of the data. It is found that the two methods relate excellently in estimating the oxygen content of samples of blood from a single individual, but that the location of the regression line changes slightly from subject to subject. It is believed that for the most part this change in the location of the regression line is due to errors in the estimation of the blood oxygen capacity, which in part are due to the day-to-day variation in the calibration of wave-length of the spectrophotometer. Variable amounts of carboxyhaemoglobin and methaemoglobin in the blood may also cause errors (Roughton *et al.*, 1944). It is also possible that the small samples of blood taken for spectrophotometric analysis are not always representative of the larger sample which is taken for manometric determination of oxygen capacity.

2. Estimation of the Arteriovenous Oxygen Content Difference in the Measurements of Cardiac Output

An experiment was designed in which two determinations of the cardiac output were made in 14 subjects, the arteriovenous oxygen content difference being determined for each estimation of cardiac output by both the manometric and the spectrophotometric method. The two measurements

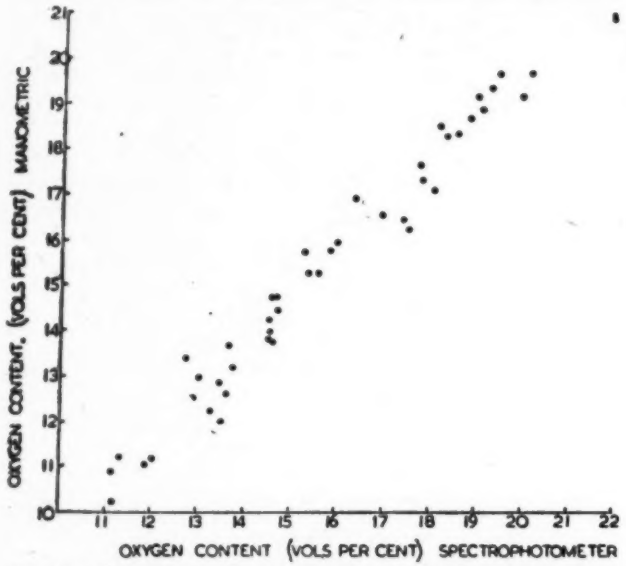

FIG. 2.—Comparison of measurements of blood oxygen content.

of cardiac output in each subject were not meant to be comparable with each other, as these subjects were not in the steady state. For each determination of cardiac output the expired air was collected for a three-minute period in a Tissot spirometer; while the gas was being collected three samples of arterial blood were collected and three samples of mixed venous blood were drawn from the pulmonary artery. The second arterial and venous samples were analysed in duplicate by the Van Slyke and Neill manometric method and the arteriovenous oxygen content difference was determined in vols. % of oxygen content. The percentage saturation of the first and third samples of arterial and venous blood was determined spectrophotometrically and the arteriovenous oxygen difference was obtained in terms of the percentage saturation. An estimate of the oxygen capacity was made by the spectrophotometer on one sample of the blood so that the arteriovenous difference of both samples could be expressed in terms of oxygen content in vols. %.

TABLE III.—*Comparison of Measurements of Arteriovenous Oxygen Content Differences*

Subject	Observation No.	Spectrophotometric Mean of two Measurements (vols. Oxygen %)	Manometric Mean of two Measurements (vols. Oxygen %)
A.118	I	5·43	5·11
	II	5·26	5·94
A.120	I	4·06	4·46
	II	4·22	4·68
A.121	I	5·85	6·13
	II	6·03	5·91
A.122	I	3·28	3·52
	II	3·55	3·90
A.124	I	2·19	2·33
	II	3·06	2·89
A.125	I	3·91	4·41
	II	4·26	3·98
A.126	I	3·33	3·41
	II	3·48	3·52
A.127	I	7·80	7·80
	II	7·49	7·10
A.128	I	7·51	6·99
	II	7·60	7·02
A.130	I	5·96	6·14
	II	6·16	6·38
A.132	I	5·62	5·40
	II	5·46	5·39
A.133	I	6·25	6·41
	II	6·44	6·70
A.134	I	4·57	4·89
	II	5·81	5·97

A.119 rejected, see text.
A.123, A.129, and A.131 were investigated for congenital heart disease: measurements of cardiac output were not made.

Fourteen subjects were catheterized in sequence, and blood and gas samples were obtained successfully in all cases. One subject (A.119) has been omitted from the series, as manometric determinations were not obtained owing to breakage of apparatus.

The measurements of arteriovenous oxygen content difference determined by the two methods in the thirteen remaining subjects are given in Table III and are plotted in Fig. 3. The relationship between the measurements made by the two methods is good and is consistent from subject to subject. The coefficient of linear correlation is r=0.98. The

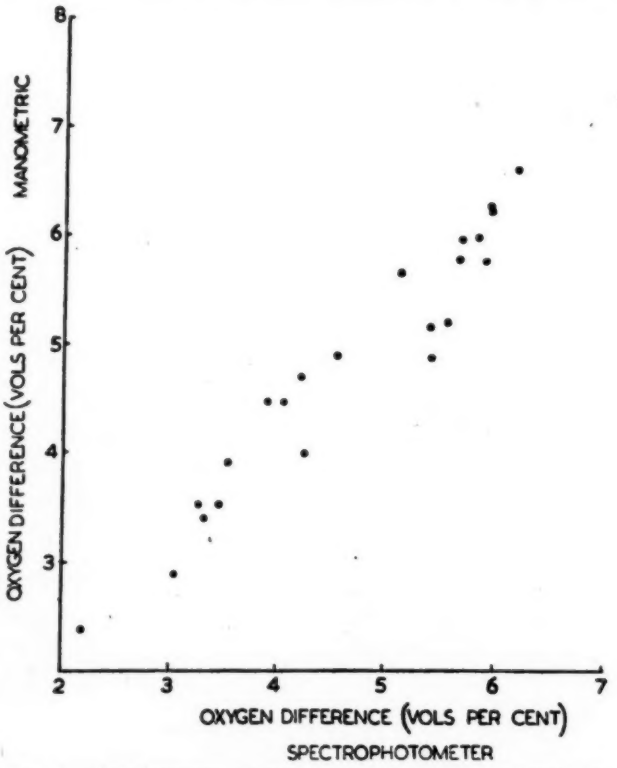

FIG. 3.—Arteriovenous oxygen content difference measured by the two methods.

regression line is given by the formula: manometric reading=0.527+(0.912×spectroscopic reading). The regression coefficient 0.912 has a standard error of 0.038 and therefore differs significantly from unity. In practice the slight modification of the result obtained by use of the regression equation is of no practical importance.

Discussion

The results reported in this paper were obtained in the first few weeks after the development of the spectroscopic technique of blood analysis in this laboratory. Comparison with manometric technique was essential at this early stage, as the reliability of the method had to be determined before it could be adopted routinely for more fundamental research. There is little doubt that if the work were to be repeated at present after the method has been in use for several months, the results would be even more satisfactory. The method has already proved itself invaluable for work that demands analysis of the oxygen content or percentage saturation of large numbers of blood samples. It is believed that further improvement in the determination of blood oxygen capacity will be obtained when a constant wave-length photometer using standard filters is employed.

Summary

A rapid spectrophotometric method of estimating percentage oxygen saturation of blood and blood oxygen content is described. The apparatus required

is simple and easily available. Two observers using the method can make duplicate estimations of the percentage oxygen saturation on 15 specimens of blood in one hour.

A comparison between results obtained by spectrophotometric analysis and by standard manometric blood–gas analysis is reported in detail.

We have much pleasure in making grateful acknowledgment to Dr. M. W. A. Gatman, of the Department of Medicine, the Royal Hospital, Sheffield, from whose work almost the whole of this technique stems, and particularly for his invaluable help and advice during the early part of this work. We would also like to thank Mr. P. D. Oldham (M.R.C.), for advice in statistical analysis, and Professor W. Melville Arnott for his helpful encouragement. Grateful acknowledgment is made of valuable financial assistance from the Research Endowment Fund of the United Birmingham Hospitals and from Messrs. Imperial Chemical Industries Limited.

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THROMBOPHLEBITIS MIGRANS AND CARCINOMA OF BODY AND TAIL OF PANCREAS

BY

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The association between thrombophlebitis migrans and carcinoma has long been known. In 1877 Trousseau gave an excellent clinical description of the recurrent painful venous thromboses affecting the arms and legs which he regarded as an important sign of carcinoma. A remarkable feature has been the frequency with which thrombophlebitis migrans is associated with carcinoma of the pancreas, particularly of the body and tail. Thoenes (1932) noted this association in three cases, and further examples were recorded by Umlauft (1933), Thomson (1938), Kenney (1943), and Jennings and Russell (1948). Sproul (1938) made a careful analysis of 4,258 consecutive necropsies and found multiple venous thromboses in 5 out of 16 cases of carcinoma of the body or tail of the pancreas and in only 3 out of 31 cases of carcinoma of the head of that organ. In addition 2 out of 81 patients with carcinoma of the lung and 2 out of 147 with carcinoma of the stomach also had multiple venous thromboses. Sproul demonstrated that in these cases there was no invasion of the veins by neoplasm nor direct compression by tumour.

By 1949 Edwards was able to analyse 29 cases of thrombophlebitis migrans associated with carcinoma—23 from the literature and 6 of his own. The site of the primary growth was in the pancreas in 16, the stomach in 4, the lung in 4, the gall-bladder in 2, and undetermined in 3. A further 8 cases were added to the literature by Smith and Albright (1952), who studied the necropsy records of 37 cases of carcinoma of the body and tail of the pancreas. The degree of preponderance of carcinoma of the body or tail of the pancreas compared with carcinoma in other sites cannot be determined from the figures available, because many workers have selected carcinoma of the pancreas for their reports. Only in Sproul's analysis has the relative infrequency of carcinoma of the body or tail of the pancreas, when compared, for instance, with carcinoma of the lung or stomach, been taken into account. The relatively frequent association of thrombophlebitis migrans with carcinoma of the body or tail of the pancreas thus becomes all the more significant.

We wish to report two further cases, drawing attention to the occurrence of arterial thrombi as well as venous thrombi and to the presence of thrombotic vegetations on the heart valves. One of our cases had a carcinoma of the tail of the pancreas, and in the other the primary growth was not found, but from the distribution of the secondary deposits it was probably also in the pancreas.

Case 1

A man aged 43 was admitted to the Manchester Royal Infirmary in December, 1951, with a six-months history of increasing weakness and recurrent attacks of thrombosis of the superficial veins of both legs and left arm. A course of anticoagulants had failed to prevent further attacks. More recently he had begun to lose weight, and shortly before admission he had some right-sided lower abdominal pain and vomiting.

On examination the patient was obviously seriously ill, with a normal temperature and a blood pressure of 170/100 mm. Hg. Thrombosed veins could be felt in both legs and the left arm. There was a persistent heavy albuminuria (10–20 g./litre). During his stay in hospital he developed a right femoral venous thrombosis and had two attacks of left-sided pleural pain. Four weeks after admission he suddenly developed a right hemiplegia and aphasia. He died three weeks later.

A blood count showed: red cells, 4,830,000 per c.mm.; haemoglobin, 14.2 g. per 100 ml.; white cells, 24,100 per c.mm., with 82% polymorphs. Microscopy and culture of the urine revealed some red cells, pus cells, cellular and granular casts, and a light growth of a coliform organism. Blood urea was 42 mg. per 100 ml., thymol turbidity 1.6 units per 100 ml., alkaline phosphatase (King–Armstrong) 28 units per 100 ml., serum albumin 3 g. per 100 ml., and serum globulin 2.9 g. per 100 ml. The blood sedimentation rate (Wintrobe) was 36 mm. in one hour. Sternal marrow examination showed slight myeloid hyperplasia with some increase of plasma cells. Intravenous and retrograde pyelograms showed no abnormality. *X*-ray examination of the lungs, skull, and pelvis was normal.

Necropsy

Naked-eye Examination.—The body was that of an emaciated man. *Venous system:* There were thrombi of varying ages in all the large and small veins of the right leg. The inferior vena cava was occluded by a thrombus to just below the entrance of the renal veins, but the latter were normal. *Heart:* On the lines of closure of the aortic cusps there were friable vegetations, the largest 1 cm. long, resembling those seen in subacute bacterial endocarditis. The underlying valve and the other valves appeared to be healthy. *Liver* (weight 1,570 g.): This contained many secondary carcinomatous deposits 2 to 15 mm. in diameter.

*In receipt of a scholarship from the Medical Research Council.

Lungs: Carcinomatous tissue was found in an apical plaque and round some of the bronchi of the lower lobes. The distribution was more suggestive of secondary spread than of primary carcinoma of the bronchus, which was carefully looked for by cutting the lungs into thin slices after fixation. There were also many infarcts and bronchopneumonia. *Brain:* The left middle cerebral artery was distended and occluded by a plug of thrombus at its first bifurcation. On section there was infarction of the white matter and cortex in the left parietal region and also in both frontal lobes. The *kidneys* and *spleen* each contained many large, old, and recent infarcts. The *pancreas* was congested. *Other organs* were within normal limits.

Histological Examination.—Carcinomatous deposits were found in the following sites: liver, lungs, tracheo-bronchial and aortic lymph nodes, and hilum of the spleen. The carcinoma was anaplastic with a hint of glandular differentiation. There was some mucin secretion. *Venous system:* The large veins mentioned above and many small ones in nearly every organ examined contained thrombi at various stages of organization. There were no metastases in or near the affected veins. A few of the sections examined showed some round-cell infiltration of the adventitia and cuffing of the vasa vasorum and small veins near by; but this reaction was no more than might be found near any thrombosed vessel. *Heart:* The vegetations were composed of eosinophilic fibrinous material covered by endothelium. They showed only a slight degree of organization, and the cellular reaction in the underlying valve was minimal. Gram's stain failed to show any organisms. The myocardium contained many minute infarcts. A few of the myocardial veins were thrombosed. *Arterial system:* Thrombi were seen in the following arteries: pulmonary, many cerebral pial, splenic, renal, pancreatic, and prostatic. *Lungs:* Numerous infarcts and thrombosed arteries and veins were present. Carcinomatous infiltration was found in the perivascular and peribronchial lymphatics and in an old apical scar. *Brain:* This contained many infarcts, probably about three weeks old. Many of the pial arteries but none of the intracerebral arteries or veins contained thrombi. *Kidneys and spleen:* Some of the infarcts were recent, but others were completely healed. *Pancreas:* Autolysed. There was patchy fibrosis, and a number of arteries and veins were thrombosed. *Other organs:* Prostate and adrenal glands contained many thrombosed veins. Pituitary gland contained a small chromophobe adenoma.

No primary carcinoma was found. Unfortunately the pancreas was sectioned in only three or four places, and a small tumour may have escaped detection. The distribution of the secondary deposits, especially the infiltration at the hilum of the spleen, suggests an origin in the tail of the pancreas.

Case 2

A woman aged 56 was first admitted to the Manchester Royal Infirmary in November, 1950, with a six-months history of weakness. Clinical examination was negative apart from a moderate anaemia (haemoglobin, 9.5 g. per 100 ml.; colour index, 0.71), which responded only slightly to iron therapy. She was readmitted in December, 1951. Six months previously she had had an attack of "pleurisy" followed by thrombosis of the superficial veins of the left leg associated with oedema, which gradually resolved in three months. One week before admission she developed phlebitis of the left forearm followed by severe abdominal pain and a rigor.

On admission the temperature was 100.4° F. (38° C.) and the patient was ill. Apart from anaemia, old thrombosed veins in the left arm, and slight albuminuria, no abnormality was found. During the next three months she developed phlebitis of the right leg and left arm in spite of a course of anticoagulants. She also had several episodes of abdominal and pleural pain accompanied by pyrexia and attacks of severe frontal headache. In February, 1952, a tender hepatic enlargement was noted and she had obviously lost weight. There were further attacks of phlebitis in both legs and increasing epigastric pain and vomiting. She gradually became more drowsy, and died in March, 1952.

A blood count showed: red cells, 4,820,000 per c.mm.; haemoglobin, 11.5 g. per 100 ml.; white cells, 13,600 per c.mm., with 81% polymorphs. Blood cultures were repeatedly negative. Thymol turbidity was 1 unit per 100 ml., alkaline phosphatase (King–Armstrong) 60 units per 100 ml., serum albumin 3.5 g. per 100 ml., serum globulin 3.2 g. per 100 ml., serum amylase 20 units per 100 ml., and serum lipase 0.6 unit per 100 ml. The electrocardiogram was normal. *X*-ray examination of the lungs, stomach, and pelvis was normal.

Necropsy

Naked-eye Examination.—The body was that of a thin woman. There was no jaundice. Oedema of the right ankle and left leg was present. *Pancreas:* The tail was expanded into a hard irregular tumour measuring 5 by 3 by 3 cm. and invading the surrounding tissue. The para-aortic glands contained macroscopic tumour deposits. *Venous system:* All the major superficial and deep veins of both legs down to the ankles were thrombosed, and a thrombus spread into the inferior vena cava to just below the entry of the renal veins. The left brachial and axillary veins and the splenic vein near the tumour were also thrombosed. *Heart:* Friable vegetations, about 3 mm. long, were found on each aortic cusp, and smaller ones were present on the atrial surface of the mitral valve. The valves appeared otherwise normal. At the apex of the left ventricle the muscle was infarcted and the endocardium was covered with ante-mortem thrombus. The coronary arteries appeared healthy. *Liver* (weight 2,250 g.): This was enlarged and to a great extent replaced by necrotic neoplastic deposits, the largest measuring 17 cm. in diameter. *Lungs:* Congestion and early bronchopneumonia were present. *Kidneys and spleen:* Each contained typical wedge-shaped infarcts, both recent and fibrotic. *Other organs:* There was a colloid goitre and an endometrial polyp.

Histological Examination.—The carcinoma in the tail of the pancreas was a moderately well-differentiated adenocarcinoma showing only a little mucin secretion. Metastases were found in the liver and the tracheo-bronchial and para-aortic lymph nodes. *Venous system:* Thrombi of varying ages were seen in the inferior vena cava, the large limb veins, and in the small veins of nearly every organ examined. There was no evidence of metastases in or near the affected veins. A few sections showed slight phlebitis and periphlebitis. *Heart:* The vegetations were similar to those of Case 1. The valves themselves were normal, apart from a little atheroma. The muscle underlying the mural thrombus was infarcted and minute infarcts were seen in the myocardium elsewhere. Many myocardial veins, venules, and several arteries were thrombosed. *Lungs:* There was bronchopneumonia. Thrombi were seen in both arteries and veins. *Brain:* Many superficial cortical arteries contained organized thrombi, and small infarcts were scattered throughout the grey and white matter. *Kidneys and spleen:* Multiple infarcts were present, some of which were several weeks old. *Head of pancreas:* This showed subacute pancreatitis. There were areas of fibrosis, possibly infarcts, as some of the arteries were occluded by thrombi. *Other organs:* There were many thrombosed veins in the thyroid and adrenal glands. The thyroid contained a non-toxic colloid nodule.

Lipase Content of Various Tissues in Case 2

Tissue	Lipase Content Units/g. (wet weight)	Normal Values Units/g. (wet weight)
Head of pancreas ..	2,800	1,110–9,000 (average 4,600)
Pancreatic tumour ..	45	——
Liver	57	10–460 (average 190)
Secondary deposit in liver	50	——

Enzyme analysis was carried out by Mr. H. Varley, of the Department of Clinical Pathology, Manchester Royal Infirmary. The tumour and its metastases were found to be non-functioning so far as lipase secretion was concerned (see Table). The serum amylase and lipase had been normal during life. (For full details of the method employed see Jackson *et al.*, 1952.)

Comment on Cases

The similarities and contrasts between these two cases are interesting. Both had widespread venous thrombosis affecting large and small veins throughout the body, thrombotic vegetations on the heart valves, and infarcts in the lungs, brain, kidneys, spleen, and myocardium. One had a well-differentiated adenocarcinoma of the tail of the pancreas with extensive metastases in the liver, whereas the other showed only a few small anaplastic secondary deposits, the primary growth being so small as to escape detection, though there was some presumptive evidence of a pancreatic origin.

Both cases showed the classical features of thrombophlebitis migrans, and because of the severity of the illness and the loss of weight an underlying neoplasm was suspected. The marked albuminuria in Case 1 was thought to be due to thrombosis of the renal veins or of the inferior vena cava above them, but this was not confirmed at necropsy. The hemiplegia in Case 1 was also ascribed to venous occlusion, but was shown to be due to blockage of the middle cerebral artery by embolus.

Discussion

Radical removal of the pancreas is now possible (Brunschwig, 1945; Whipple, 1946; and others); and early diagnosis of carcinoma of that organ becomes increasingly more important. Clinically this is notoriously difficult when the neoplasm is situated in the body or tail of the pancreas (Ransom, 1935; Duff, 1939), and any sign which may attract attention to the condition is important. In a number of patients migratory thrombophlebitis is the presenting sign of the disease; indeed, Edwards (1949) found the association so striking that he advocated laparotomy in all cases of thrombophlebitis migrans if no neoplasm was discovered by the usual investigations. The main conditions which have to be excluded before such a course is taken are thromboangiitis obliterans and so-called idiopathic thrombophlebitis migrans. The migratory phlebitis of the deep and superficial limb veins with accompanying oedema, occasional visceral thrombosis, pulmonary emboli, and variable general reaction are so similar in the idiopathic thrombophlebitis and that associated with carcinoma that the two conditions cannot be distinguished until obvious signs of neoplasm have appeared.

The value of biopsy of a vascular bundle in the differential diagnosis cannot yet be established, although thromboangiitis obliterans can usually be excluded. No biopsies have been reported from cases with multiple venous thromboses and carcinoma. From post-mortem studies it seems that the slight inflammatory reaction such as was occasionally seen in our sections is very similar to that reported by Barker (1936) in the idiopathic variety. To attempt to establish the diagnosis laparotomy may have to be resorted to, but in the few cases in which this has been done metastatic spread had already taken place (Edwards, 1949).

It has repeatedly been stated that the recurring thromboses affect the venous system exclusively, with the exception of the pulmonary arteries, which may contain emboli. In both our cases there were infarcts in many organs, due to arterial occlusion. In view of the presence of friable vegetations on the heart valves, embolization seems the most likely explanation, but there was such widespread occlusion of small arteries, especially in both brains, that the possibility of local arterial thrombosis should be considered. Infarcts have been described by various workers, but have always been ascribed to venous occlusion. The vegetations on the aortic and mitral valves appear to be another manifestation of the thrombotic tendency. Sproul (1938) reported them in four of her five cases of multiple venous thrombi with carcinoma of the body or tail of the pancreas, and they have also been described in idiopathic thrombophlebitis migrans (Hirschhorn *et al.*, 1939; Swirsky and Cassano, 1943). The vegetations were macroscopically and histologically similar to those described by Gross and Friedberg (1936) as non-bacterial thrombotic endocarditis.

The theories put forward to explain the pathogenesis of the multiple venous thromboses are not satisfactory. The subject has been reviewed by Sproul (1938) and by Kenney (1943), and little has since been added. No local causes such as neoplasm or inflammation (other than the slight cellular reaction thought to be the consequence rather than the cause of thrombosis) have been demonstrated histologically. Attention has been focused on those cases of thrombophlebitis migrans with carcinoma of the body or tail of the pancreas and the possibility of increased or abnormal enzyme secretion, which has been thought to alter the coagulability of the blood. However, no abnormality has been demonstrated in the blood-clotting mechanism, and anticoagulants have had no effect on the course of the disease. So far as we are aware, the only enzyme study actually carried out in this disease has been in our second case, in which the tumour and its metastases were inactive so far as lipase secretion was concerned. It must be remembered that any theory concerning the pathogenesis of thrombophlebitis migrans with carcinoma must explain those cases in which the primary growth arises in organs other than the pancreas.

Summary

Two cases of thrombophlebitis migrans with carcinoma are reported. In one the primary growth was in the tail of the pancreas, and in the other the site was undetermined. The association between carcinoma of the body or tail of the pancreas and thrombophlebitis migrans is emphasized.

The occurrence of non-bacterial thrombotic endocarditis in this syndrome is stressed, and attention is drawn to the fact that the clinical picture may consist of arterial embolic as well as venous thrombotic episodes.

The possibility of arterial as well as venous thromboses is considered.

The lipase content of one of the tumours and its metastases was estimated and found to be negligible.

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MULTIPLE MYELOMATOSIS WITH HAEMATEMESIS AND MELAENA

BY

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Multiple myelomatosis is a disease of protean manifestations, the diagnosis of which depends on the accurate correlation of clinical signs, symptoms, and the results of pathological and radiological investigations. Excellent general reviews of the subject are to be found in papers by Bayrd and Heck (1947), Geschickter and Copeland (1928), and Lichtenstein and Jaffé (1947) amongst others.

The disease is commonest in the male sex between the ages of 40 and 70. The main clinical features are: (*a*) pain, at first vague and intermittent, located in the affected bones (often most severe in the lumbar vertebrae); (*b*) tumour deposits in the bones, giving rise to localized swellings, pathological fractures, and deformities; (*c*) anaemia; (*d*) purpuric phenomena; and (*e*) "albuminuria." Radiographs of the bones often show a characteristic picture, with multiple "punched-out" areas of rarefaction.

The principal abnormalities detectable in the laboratory are hyperproteinaemia with qualitative and quantitative alterations in the plasma proteins, autohaemagglutination, the presence of Bence Jones protein in the urine, and myeloma cells in the bone marrow. These cells are sometimes present in the peripheral blood, which may show a raised serum calcium with a normal phosphate level.

The diagnosis of cases with widespread skeletal involvement is usually fairly easy, though osteitis fibrosa cystica may on occasion produce a very similar picture, especially when, as sometimes happens, the biochemical findings are equivocal. When there are no obvious bony lesions diagnostic errors are frequent, such cases being labelled "chronic nephritis," "neuralgia," "arthritis," etc.

The following cases illustrate an unusual presentation with a clinical picture suggestive of peptic ulcer.

Case 1

A man aged 62 was admitted to hospital on September 19, 1947. In the previous June he had noticed that he was losing weight and had become rather lethargic. One month later he had an epistaxis. In August he consulted his family doctor on account of increasing dyspnoea and was treated for anaemia with iron injections. Later he developed anorexia, and on September 1 vomited several times.

On admission he was seen to be pale and his skin had a faint yellowish tinge. His gums were bleeding slightly and his spleen was just palpable. His blood pressure was 90/70. The blood picture was as follows: Hb, 28%; red cells, 1,190,000; white cells 6,700 (74% neutrophils); nucleated red cells present in the peripheral blood but no myeloma cells.

A transfusion of 2 pints (1.1 litres) of Group O Rh-positive blood was given. The haemoglobin level rose by 6% and then fell. A fractional test meal was performed and blood and starch were found in all specimens. The stools contained occult blood. A tentative diagnosis of gastric ulcer or carcinoma was made and a second transfusion of 2 pints (1.1 litres) of blood was given. Gingival bleeding continued and an ascorbic acid saturation test showed a deficient output; this was corrected by vitamin therapy.

On October 8 the patient complained of severe abdominal pain and nausea, passed a melaenatous stool, and vomited about a pint (570 ml.) of blood-stained material. On the 9th he had another haematemesis and on the 10th his stool gave a positive reaction for occult blood. At this stage it was noted that his red cells were strongly clumped *in vitro* by his own serum, and cross-matching of blood for transfusion was hindered by massive compound rouleaux formation when donor erythrocytes were added to his serum. Despite these difficulties 5 pints (2.8 litres) of compatible blood was given by slow drip transfusion and the haemoglobin had risen to 62% by October 16. Thereafter gingival bleeding and occasional vomiting of altered blood continued and his condition gradually deteriorated. He died in coma on November 3.

Post-mortem Examination.—Only the salient features are noted. There was a pathological fracture in the body of the sternum at the junction of the upper two-thirds and lower one-third, the bone being expanded by red gelatinous material. The calvarium contained numerous dark red circular deposits of varying size, the largest being ½ in. (1.3 cm.) in diameter, with thinning of the overlying diploë. The alimentary tract contained pin-point haemorrhages and areas of congestion, particularly conspicuous in the stomach, duodenum, and caecum. The spleen was small and soft. The myocardium was pale and flabby. The kidneys were pale and showed some reduction of their cortical tissue. There was a terminal hypostatic pneumonia. Films made from the marrow of the sternum, femur, and vertebrae showed large numbers of myeloma cells.

Case 2

A man aged 59 had been losing weight for twelve months and during this time had had occasional abdominal pain and discomfort. On January 30, 1952, he suddenly vomited altered blood and passed large quantities of dark tarry faeces, after which he felt very faint and weak. He was admitted to hospital on the following day.

On admission he was seen to be pale and shocked; his blood pressure was 90/70; haemoglobin, 34%; blood urea, 59 mg. per 100 ml.; serum potassium, 15 mg. per 100 ml. Transfusion was started and a total of 9 pints (5.1 litres) of blood was given over the next twenty-seven days, the haemoglobin rising to 63%, with great improvement in the clinical condition. The radiological appearances following a barium meal were suggestive of duodenal ulceration. By February 17 faecal tests for occult blood were negative. The patient was sent home to convalesce with a view to future surgery. A few days later he noticed that he was passing very little urine, and the little he did pass appeared to contain blood.

He was readmitted to hospital on March 20. He looked pale and ill. His face was rather puffy and there was some pharyngeal inflammation. His blood pressure was 135/70; temperature 99.4° F. (37.4° C.). A clinical diagnosis of nephritis was made. Laboratory investigations showed albumin and blood in the urine, with hyaline and granular casts in the centrifuged deposit; Hb 50%; blood urea, 73 mg. per 100 ml. The following day the patient became drowsy and anorexial. He gradually passed into a uraemic state with a brown furred tongue, his blood urea steadily rising and the haemoglobin falling. Further urine examinations revealed red blood cells in the centrifuged deposit. Transfusions were given to combat the anaemia, and on April 16, during the course of routine cross-matching and grouping, massive autohaemagglutination of his red cells was noted. On the 19th a plasma protein analysis gave the following figures: total protein 12.4 g. (albumin 2.5 g., globulin 9.9 g.). The white blood cells numbered 22,000 per c.mm. (11% myeloma cells). Platelets were scanty in the films and a count revealed 107,000 per c.mm. The patient died on April 22. The final blood investigations shortly

before death showed Hb, 36%; urea, 448 mg. per 100 ml.; platelets, 34,000 per c.mm.; 20% myeloma cells in differential white blood count.

Post-mortem Examination.—The main features were as follows. The bone marrow of the skull was diffusely infiltrated by dark red gelatinous material, and a similar infiltration was found in the vertebrae and sternum. In the femoral marrow, however, the picture was different; discrete tumour nodules were found, separated by areas of relatively normal-looking marrow. There were petechial haemorrhages in the gastric mucosa; no ulcers were found, but the intestinal tract contained a moderate quantity of dark tarry faecal matter. The lungs showed basal bronchopneumonia. Both kidneys were large and pale. Their capsules stripped easily and the external surfaces were smooth and congested. The cut surfaces had a pale yellowish, slightly greasy appearance, and the distinction between cortex and medulla was much less clear-cut than normal. The mucosa of the bladder showed petechial haemorrhages and the left lobe of the thyroid gland contained a small colloid adenoma with areas of haemorrhage in its substance.

Histology.—Sections from the gelatinous areas in the marrow of the sternum, skull, and femur showed a diffuse and uniform replacement of the normal marrow tissues by closely packed myeloma cells. The sinusoids of the liver and spleen contained varying numbers of myeloma cells. The kidneys showed blockage of large numbers of their tubules by hyaline eosinophilic casts; focal infiltrations of myeloma cells were present.

Discussion

These two cases of multiple myelomatosis show gastrointestinal features seldom described in the literature. Geschickter and Copeland (1928) noted nausea, vomiting, and colic in 20% of their cases, but haematemesis and melaena, in contrast to bleeding from the nose and gums, are rare. Bertoye (1904) gave a lengthy account of a case in which two attacks of haematemesis occurred, the second being fatal. Moss and Ackerman (1946) described an example of "plasma cell leukaemia" with tarry and blood-streaked stools, and they quoted a case of Askanazy's which showed haemorrhage from the gastric mucosa. Cases such as these, however, are few and far between, and the very infrequency of gastro-intestinal haemorrhage in myelomatosis may easily lead the clinician to make an erroneous diagnosis of peptic ulcer or gastric neoplasm. The correct diagnosis may be made in the laboratory, and the patient may be spared an unnecessary operation, if certain clues previously indicated are followed up.

Of these, the ones most likely to be detected initially are the phenomena of autohaemagglutination and massive rouleaux formation, which may give rise to great difficulties in cross-matching blood for transfusion and in performing blood counts, particularly when Hayem's diluent is used for red-cell estimations. Rouleaux formation was found by Bayrd and Heck (1947) in 60% of their cases, and, in common with other authors, they noted that it was correlated with a raised serum globulin level and an increased erythrocyte sedimentation rate. "Streakiness" of blood films may also be noted in such circumstances. With regard to the sedimentation rate a peculiar discrepancy between the results obtained by the Wintrobe and Westergren techniques is apparent in some cases, as the former may give figures within the normal range when the Westergren result is 100 mm. in one hour, or even higher.

The finding of any of these haematological abnormalities should suggest the possibility of myelomatosis, and further investigations should be made. From the practical standpoint the next most useful procedure is the estimation of the plasma proteins. In this laboratory the copper sulphate specific gravity technique is used as a rough preliminary test. Hyperproteinaemia, with reversal of the albumin/globulin ratio, is often found. Bayrd and Heck (1947) found it in 73% of cases and Gutman and Gutman (1936) in 35 out of 57 cases. Sometimes only the globulin fraction is increased, the total protein content of the plasma being within normal limits. Recent work by Maclagan *et al.* (1952) indicates that such alterations in the plasma protein pattern lead, apparently in a definite sequence, to abnormal results being obtained from various liver-function tests. The total serum globulin and the albumin/globulin ratio are first to be affected, followed by the ammonium sulphate turbidity, zinc sulphate turbidity, serum colloidal gold, and thymol turbidity and flocculation reactions, in that order.

Examination of the urine for Bence Jones "protein" should, of course, be carried out, but it must be appreciated that it may be present only intermittently. Technical difficulties are sometimes encountered, especially when the urine contains only small amounts of the substance, or when large quantities of ordinary albumin are also present. Discombe *et al.* (1937) have described reliable methods for overcoming these difficulties.

Myeloma cells may be detected in the peripheral blood, though the frequency with which they are found is rather variable. Lichtenstein and Jaffe (1947) found 2 out of 35 cases, and Morissette and Watkins (1942) 41 out of 56 cases. Except in the rare "plasma cell leukaemia," their presence in the peripheral blood tends to be a late, or terminal, phenomenon. Bone-marrow biopsy will enable a conclusive diagnosis to be made if a myelomatous area can be located.

With regard to the cytological features, several authors have described variations in the myeloma cells; thus it is commonly recognized that there is a "small-cell" type, in which the tumour cells resemble plasma cells, and a "large-celled" type, in which the cells have large, pale, round, oval, or reniform nuclei showing fine chromatin stippling. There may be rod-shaped bodies of variable staining and vacuoles in the cytoplasm. The distinctive features of myeloma cells are best demonstrated by special staining techniques, such as the Unna–Pappenheim method.

In conclusion, it should be mentioned again that in some cases of myelomatosis an erroneous diagnosis of "nephritis" may be made, as happened initially in Case 2 above, during his second admission to hospital. Though the only direct effect of myelomatosis on the kidney seems to be the deposition of proteinaceous casts in the tubules (Bell, 1933) the clinical picture is not uncommonly complicated by coexisting arteriosclerosis or pyelonephritis. Usually, however, the correct diagnosis can be made by performing the cardinal laboratory investigations outlined above.

Summary

Two cases of multiple myelomatosis, with haematemesis and melaena, are recorded. The main laboratory investigations necessary for the diagnosis of the disease are outlined.

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INTRAVENOUS IRON IN RHEUMATOID ARTHRITIS: POSSIBLE PROGNOSTIC FACTORS

BY

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The anaemia which often accompanies rheumatoid arthritis is usually improved by intravenous iron therapy. Some patients, however, derive no benefit, and, in view of the not infrequent technical difficulty of intravenous injections in these cases, it would be useful if they could be easily recognized. Useless and perhaps awkward therapy could thus be avoided and blood transfusion given at once if, for example, orthopaedic procedures were imminent.

To try to discover factors of possible prognostic value, the results of a variety of observations upon patients who received intravenous iron have been assembled, but no satisfactory test has emerged.

Material and Methods

Only data from anaemic cases of uncomplicated rheumatoid arthritis are included. Cases receiving treatment other than simple analgesics and physiotherapy were excluded. The effect of treatment was gauged from the haemoglobin value three months after treatment; figures of 14 and 12.5 g. per 100 ml. were taken as the lower limit of normality for men and women respectively, and an increase of 1.5 g. or more per 100 ml. was regarded as "material improvement." The dose given was one and a half times the amount calculated to raise the haemoglobin to 100% (14.8 g.), on the basis that 100 mg. of iron raises the level by 4%. Injections were given thrice weekly.

The following techniques were used:

Red-cell count: the top and bottom rows of each side of an improved Neubauer chamber were counted—that is, four rows of five large squares.

Haemoglobin: alkaline haematin, comparing photometrically with Gibson and Harrison's artificial standard.

Haematocrit: Wintrobe's tubes, spun to constant volume at 1,500 g (about 3,200 r.p.m.).

Sedimentation rate: Westergren method.

Plasma iron: Kitzes, Elvehjem, and Schuette (1944).

Free erythrocyte protoporphyrin: Grinstein and Watson (1943), comparing the fluorescence of the final extract in 5% HCl with that of a standard safranine solution (100 mg. per litre). This standard had previously been compared with pure protoporphyrin.

Iron-binding capacity of the serum: Rath and Finch (1949).

Serum proteins: biuret method for total protein and albumin after precipitation of globulin by half-saturated ammonium sulphate.

Comment upon Results

The effects of intravenous iron upon haemoglobin levels are shown in Table I. Roughly one-quarter of the patients derived no material benefit, and a return to normal levels was more frequent in the women than in the men.

TABLE I.—*Effects of Intravenous Iron on Haemoglobin Levels*

	No. of Cases	Haemoglobin Three Months after Treatment		
		Normal	Improved	Unchanged
Men	14	1	9	4
Women ..	36	14	13	9

In Table II the cases are grouped according to the effect of treatment, the results of various investigations being summarized for each group. It is obvious that with every investigation some overlap between the groups occurred and no single characteristic infallibly distinguished potential failures or successes.

As noted by previous workers, a good response to intravenous iron was more likely when the disease was relatively inactive, and was unlikely if very severe disease with much constitutional disturbance was present. Nine out of 15 "successes" had sedimentation rates below 30 mm. in one hour, and no patient with a sedimentation rate below this figure failed to achieve normal levels; conversely, in only one "failure" was the rate below 45 mm. A high rate did not, however, necessarily preclude a good result, for patients with relatively slight constitutional disturbance usually responded well, whatever the laboratory findings. In fact, the amount of subcutaneous fat was as good a guide to the result of treatment as any other.

None of the indices, mean corpuscular volume, mean corpuscular haemoglobin, or mean corpuscular haemoglobin concentration regularly distinguished failures or successes, though in each case the mean values were lowest in the group whose haemoglobin became normal. The haemoglobin levels of the four cases showing microcytosis all returned to normal, as did the levels of the six cases having grossly diminished mean corpuscular haemoglobin (<21 $\mu\mu$g.).

Plasma iron and the degree of saturation of the iron-binding protein were of no prognostic value. A raised total iron-binding capacity was found in nine women, all of whom achieved final haemoglobin values above 12 g. per 100 ml.; normal or reduced iron-binding capacity showed no significant correlation with the result of therapy. To try to assess the rate of removal of injected iron from the blood stream, plasma iron was estimated half an hour and three hours after a dose of 50 mg. intravenously. At both times there was a suggestion that the "failures" removed the metal more quickly, but the differences were slight and overlap was considerable. Only the three-hour figures appear in Table II.

Serum albumin and globulin gave no prognostic guidance. Estimation of free erythrocyte protoporphyrin was also use-

TABLE II

Investigation	Haemoglobin Unchanged			Haemoglobin Improved			Haemoglobin Normal		
	Mean	Range	Cases	Mean	Range	Cases	Mean	Range	Cases
Disease activity:									
Slight			2			6			10
Marked			11			16			5
Sedimentation rate (mm./1 hr.)	67	30–125	13	68	15–110	22	39	11–108	15*
M.C.V. (μ^3)	89·5	79·5–102	11	92	83–100	11	78·5	64·5–92·5	9
M.C.H. ($\mu\mu$g.)	26·0	21·6–30·4	11	25·1	23·2–27·8	11	20·8	14·6–26·2	9†
M.C.H.C. (%)	28·9	26·0–31·7	13	27·5	25·7–29·8	17	25·7	22·4–29·5	14
Plasma iron (μg./100 ml.)	33	12–82	13	36	7–91	21	31	7–66	14
T.I.B.C. (μg./100 ml.)	320	185–415	7	362	255–475	13	448	335–570	10‡
Saturation of iron-binding protein (%) ..	9	4–16	7	9	3–17	13	7	2–11	10
3-hr. plasma iron rise (μg./100 ml.) ..	149	80–205	8	251	110–355	8	195	165–240	6
Serum albumin (g./100 ml.)	4·5	4·0–5·4	5	4·4	3·6–5·6	13	4·5	3·8–5·2	8
,, globulin ,, ...	3·0	2·1–3·7	5	3·3	1·9–4·9	12	2·4	1·8–2·7	8
Free erythrocyte protoporphyrin (μg./100 ml.)	16, 32, 37, 50, 52, 130, 304		7	28, 34, 39, 41, 42, 47, 48, 50, 80		9	20, 32, 162, 166, 1,100		5

* 9 were <30 mm./1 hr. † 6 were <21·5 $\mu\mu$g. ‡ 6 were >430 μg./100 ml.

less, normal and raised values occurring in all groups. The raised values always became normal after iron therapy, however, even in the absence of a material rise in haemoglobin level.

Conclusions

In 50 cases of rheumatoid arthritis, failure of their anaemia to respond to intravenous iron could not be predicted from the results of any of the investigations examined.

Return of the haemoglobin to normality occurred regularly when one or more of the following were present: sedimentation rate below 30 mm. in one hour, microcytosis, gross hypochromasia, and raised total iron-binding capacity of the serum.

The haemoglobin, however, returned to normal or improved greatly in many cases which showed none of the above criteria.

It appears that intravenous iron is always worth trying in the anaemia of rheumatoid arthritis, except when severe constitutional disturbance or the imminence of surgery makes preferable the rapid rise in haemoglobin which follows blood transfusion.

My thanks are due to Dr. G. D. Kersley for his helpful criticism and advice, and for allowing the investigation of patients in his care. I am indebted to Professor C. Rimington for providing some pure protoporphyrin and to the Empire Rheumatism Council, whose grant for the purchase of a fluorimeter made the porphyrin part of this work possible.

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ACTINOMYCOTIC PYAEMIA

BY

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Human infection with filamentous organisms of the group *Actinomyces* is an uncommon but well-recognized condition. In most cases the anaerobic species *Actinomyces israeli* is the causal organism, and infection with it usually results in localized lesions in the neck or abdomen (Cope, 1938), although on rare occasions generalized pyaemic spread occurs with multiple abscesses throughout the body (Israël, 1878; Harbitz and Grondahl, 1911; Shrewsbury, 1928). In a much smaller number of cases infection is due to aerobic filamentous organisms, most commonly *Nocardia asteroides*, which usually cause pulmonary lesions and are often associated with systemic spread (Biggart, 1934; Benbow *et al.*, 1944; Kirby and McNaught, 1946). The relative frequency of infection with the different organisms is difficult to determine, since few detailed bacteriological studies are reported and diagnosis has often been based upon the appearance of a filamentous organism in a stained film or on the presence of "granules" in pus.

Systemic spread was equally fatal in both types of infection until the use of antibiotics in treatment, and precise bacteriological diagnosis was therefore not important. Since the behaviour of the two species towards antibiotics is different, cultural identification of the organism has become imperative, particularly in view of the possibility of complete recovery even after prolonged illness and in the presence of pyaemic dissemination as in the following case.

Case Report

The patient, a 50-year-old director, first noticed vague malaise, with loss of appetite and weight, in March, 1950. In August he had a mild fever for several days, which subsided without treatment. In October he developed left-sided chest pain, and on admission to hospital two weeks later was pyrexial and ill, but, apart from some loss of weight, there were no abnormal physical signs. A chest *x*-ray film showed some loss of translucency at the left costo-phrenic angle. A blood examination showed: red cells, 4,100,000 per c.mm.; Hb, 84% (12 g. per 100 ml.); white cells, 6,400 per c.mm.; blood urea, 36 mg. per 100 ml.; erythrocyte sedimentation rate (E.S.R.), 24 mm. per hour (Wintrobe). The pyrexia subsided without treatment after a week in hospital and the patient was discharged.

He remained unwell and continued to lose weight. In April, 1951, he had a further attack of chest pain, which improved after several days' treatment with penicillin. On May 24 he suddenly developed a fluctuant painful swelling in the left arm, and at about this time developed several painful whitlows. The swelling in the arm was aspirated, but the contents were sterile on culture; it continued to discharge for about two months. A chest *x*-ray film showed no change since October, 1950. On July 5 a painful swelling appeared in the left calf, and smaller swellings occurred on his feet and left arm before readmission to hospital on July 26. He was then febrile, ill, and wasted, and had lost 3 stone (19 kg.) in weight. There was a productive cough, with abundant purulent sputum; numerous rales and crepitations were audible at both lung bases. The liver and spleen were not palpable, and the abdomen appeared normal. The cardiovascular system was normal. A very tender, fluctuant swelling (5 by 2 by 2 cm.) was present in the left gastrocnemius; and a smaller nodule (about 2 by 1 by 1 cm.) was felt in the muscles of the left forearm. There were two flat greyish lesions about 0.2 cm. diameter in the skin at the margin of the nail bed on the left hand, and larger bluish grey lesions in the skin over the right tibia, on the medial surface of the right foot, and on the right heel. These lesions consisted of a central zone of necrotic skin (the largest was 2 by 1 cm.) surrounded by a thin, slightly raised red area and a wider diffuse zone of induration tender to touch.

A blood count showed: red cells, 4,200,000 per c.mm.; Hb, 88% (12.2 g. per 100 ml.); white cells, 7,400 per c.mm. (89.3% polymorphonuclear leucocytes). The E.S.R. was 129 mm. per hour (Westergren), and the chest *x*-ray film now showed diffuse miliary shadowing throughout both lung fields. The urine was normal. Aspiration of the calf abscess produced about 0.5 ml. of thick blood-stained material, containing numerous pus cells, and a Gram-positive filamentous branching organism with many smaller Gram-negative bacilli. Similar filamentous organisms were seen in the pus from all the superficial lesions, and were also present in the sputum, which contained yellowish granules. Exploration of the calf showed a thick-walled abscess cavity, containing about 40 ml. of viscous blood-stained pus in which were numerous yellow granules, which showed typical "ray fungus" on microscopical examination. The patient was first treated with intramuscular streptomycin, 2 g. a day, since infection with *N. asteroides* seemed probable. He remained pyrexial, several new lesions appeared in the extremities, and after one week 2 mega units of penicillin daily were given together with the streptomycin. The latter was replaced after 14 days' treatment by "sulphatriad," 3 g. daily, in view of the isolation of *A. israeli* from the pus and sputum, and the penicillin was increased to 4 mega units daily.

The pyrexia continued for a further two weeks and then subsided slowly. Several painless nodules appeared in the subcutaneous tissues on the arm and leg, but resolved without causing abscesses. No fresh lesions appeared after three weeks' treatment, and those that were already present healed; the sputum diminished greatly. There was no change in the radiological appearances of the chest, and the E.S.R. remained raised for several months. After about five weeks' treatment the patient had improved and had gained weight for the first time for two years. On discharge from hospital on October 17 his weight was 8 st. 10 lb. (55.3 kg.), there was neither cough nor sputum, and no abnormal physical signs were present. The chest *x*-ray film was unchanged and the serum proteins and sedimentation rate were still abnormal.

Daily injections of 1 mega unit of penicillin together with 2 g. of sulphatriad by mouth were continued for a further three months at home, and these were finally stopped after six months' treatment. The serum proteins and liver-function tests were still abnormal, but thereafter improved steadily. The patient returned to work in April, 1952, and has since remained well. The chest film still showed some miliary shadowing in September, 1952, although this was less pronounced.

Bacteriology and Serology

A filamentous organism was isolated from the pus from the abscesses in the gastrocnemius and on the feet and from the sputum. On primary culture in Brewer's medium it grew well in anaerobic conditions in 10% CO_2 at 37° C. The organism also grew aerobically in 10% CO_2 when it dissociated to give a rough and a smooth strain. The latter was stable, but the rough strain continued to dissociate in repeated subculture.

The primary strain, under anaerobic conditions, always gave a heavy growth of rhizoid, adherent colonies, which were just visible to the naked eye at 24 hours' incubation. After six days the colonies were 1–1.5 mm. in diameter. This strain, grown aerobically, gave a less luxuriant growth, the colonies after six days being only 0.3–0.5 mm. in diameter. The smooth dissociated strain, under aerobic conditions, gave a much more luxuriant growth than did the rough strain.

Impression colonies of both strains showed the typical appearance of actinomyces. The rough strain was a filamentous organism which showed a typical branch formation, while the smooth strain consisted almost entirely of rod-shaped organisms. Both strains passed through the life cycle described in the case of *A. israeli* (syn. *bovis*) (Morris, 1951).

The fermentation reactions of the organisms with carbohydrates are shown in Table I, and are compared with a summary of the widely differing reactions of *A. israeli* (*bovis*) previously reported. These are listed in detail by

Table I.—*Biochemical Reactions of the Organism*

	Dextrin	Rhamnose	Dulcitol	Xylose	Starch	Aesculin	Sorbitol	Inulin	Raffinose	Arabinose	Salicin	Maltose	Mannitol	Sucrose	Lactose	Glucose	Glycogen
Summarized results (Sullivan *et al.*, 1940)	—	—	—	—	v	—	—	v	v	—	v	+	v	+	+	+	v
Strain under investigation ..	*	—	—	—	—	—	—	+	+	—	*	—	*	+	+	+	+
	—	—	—	—	—	—	—	+	+	—	+	—	+	+	+	+	+

+ = Acid production. — = No reaction. v = Variable reaction. * = Human strains only.

Sullivan and Goldsworthy (1940). Phosphatase was produced (Morris, 1952). Acid but no gas was produced in litmus milk. Catalase was not demonstrated in the presence of hydrogen peroxide. Hydrogen sulphide was not produced, and nitrates were not reduced. No growth was obtained in 10% bile broth, in broth at *p*H 9.6 or *p*H 5, or in 6.5% NaCl broth. The organism failed to grow at room temperature or at 45° C. Indole and Vosges–Proskauer tests were negative, and the methyl-red test was weakly positive.

Complement-fixation tests have been shown to be satisfactory in the study of the *Actinomyces* (Morris, 1952). The following titres were obtained with the organism: human-strain antiserum, 1 in 1,280; bovine- strain antiserum, 1 in 640; and patient's serum, 1 in 1,280.

Discussion

There was no definite evidence to indicate the time of first infection in the present case, although it was clear that localized pulmonary infection preceded the pyaemic abscesses, which were accompanied by miliary spread throughout both lungs. Disseminated actinomycosis seems to arise from pulmonary infections, since in the more common type of abdominal and cervical lesions localization with extensive fibrosis is the characteristic feature. The nature of the primary pulmonary changes in the present case was not known, but may have been insignificant, since *A. israeli* has been isolated from the sputum in cases of chronic bronchitis (Kay, 1948).

The peripheral lesions in the present case seem to have been confined to muscle, subcutaneous tissue, and skin, for no evidence was found of spread to internal organs. This curious localization has been noted in several necropsy reports in the literature. The small necrotic subcutaneous lesions were strikingly painless, and were similar to those described in nocardial infections by Kirby and McNaught (1946). The organism showed the typical cultural and life-cycle appearances of *A. israeli*, although it was unusual in that it grew freely in aerobic culture in CO_2. This may have determined the mode of spread, since it has been claimed that systemic infection rarely, if ever, occurs with anaerobic organisms (Weed and Baggenstoss, 1949). The filaments were accompanied by a small Gram-negative bacillus in the stained film which on anaerobic culture was shown to be *Bact. actinomycetem comitans*. This organism has been claimed to be invariably associated with anaerobic actinomycetes, even in peripheral closed abscess (Holm, 1950), and to distinguish these lesions from those produced by nocardia, in which it is not found.

Serial analyses of the serum proteins were performed by Dr. J. Hardwicke. Total serum protein was estimated by the biuret method (Weichselbaum, 1946), fibrinogen by nitrogen estimation on fibrin clot (Peters and Van Slyke, 1932), and differential serum proteins by a modified technique of electrophoresis on filter paper (Kunkel and Tiselius, 1951).

Table II.—*Plasma Protein Estimations*

Date	Total Protein (g./100 ml.)	Albumin (g./100 ml.)	Globulin (g./100 ml.)				Fibrinogen (g./100 ml.)
			α_1	α_2	β	γ	
31/6/51	5·7	1·0	0·3	0·6	0·6	3·2	0·47
8/10/51	8·0	1·9	0·3	0·7	0·6	4·5	0·55
30/11/51	9·0	2·5	0·4	1·0	1·6	3·5	0·58
22/1/52	8·6	2·4	0·3	1·1	1·2	3·6	0·69
21/3/52	8·2	4·4	0·4	0·9	0·7	1·7	0·52
4/9/52	7·5	5·0	0·2	0·5	0·6	1·2	0·43
Mean normal values by method ..		4·5	0·2	0·6	0·6	0·8	0·34

On admission the total protein was low (Table II), the fibrinogen slightly raised, and the γ-globulin greatly raised. During treatment the total protein rose, with an increase in all fractions, but the high γ-globulin concentration did not fall appreciably until penicillin was discontinued, several months after clinical recovery. The serum albumin remained low until the γ-globulin fell, suggesting a possible inverse relationship between these fractions.

Similar changes in the serum proteins in chronic infections have been reported (Marrack and Hoch, 1949), and high total globulins associated with abnormal liver-function tests were described in a case of actinomycosis by Torrens and

Wood (1949). This high γ-globulin, which may be a reflection of antibody formation, probably accounts for the abnormal liver-function tests. γ-globulin has also been shown to increase the E.S.R. (Hardwicke and Squire, 1952), which in this case remained high long after clinical recovery, and made it, therefore, an unsatisfactory index of progress.

The successful treatment of localized actinomycosis with antibiotics has been widely reported, but recovery after pyaemic dissemination seems to be extremely rare. *A. israeli* is sensitive to penicillin and rarely develops resistance (Boand and Novak, 1949); streptomycin resistance usually develops rapidly. Sulphonamides are usually given with penicillin, although there is no direct evidence of synergistic action between these substances. In the present case penicillin and sulphatriad were used in combination for six months; the streptomycin given in the seven days before the identity of the organism was established had little effect. Several cases have been reported, however, of the successful use of streptomycin in those rare instances in which the strain is penicillin-resistant (Torrens and Wood, 1949; Pemberton and Hunter, 1949). The majority of strains of *Nocardia* are penicillin-resistant (Drake, 1946), but have been shown to be highly sensitive to sulphonamides and moderately sensitive to streptomycin (Glover *et al.*, 1948).

Summary

A case of generalized pyaemia with miliary pulmonary infiltration due to *Actinomyces israeli* is described.

The organism, described in detail, was unusual in showing free growth in aerobic culture in CO_2.

During the illness gross abnormalities of the serum proteins were observed by electrophoresis on paper strips.

The patient was treated with penicillin and sulphonamides for six months and made a full recovery.

We wish to acknowledge our gratitude to Dr. Ernest Bulmer for permission to publish this case, to Mr. V. Brookes for the surgical details, and to Dr. J. Hardwicke, in receipt of a Medical Research Council grant in the Department of Experimental Pathology, University of Birmingham, for the detailed protein studies.

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At the official opening of the 38th Nurses and Midwives Conference and Exhibition in London on October 12, Mrs. Iain Macleod said that, although there were more nurses in the Health Service than ever before (147,000 full-time and 27,500 part-time, as compared with 118,000 and 17,000 respectively in June, 1948), there was still a great need for more nurses in mental hospitals and tuberculosis wards. This difficulty was being partly overcome, as more nurses were now being trained in sanatoria, but there was still a shortage in mental institutions.

ACTION OF THIOURACIL AND THYROXINE ADMINISTRATION ON ADRENAL FUNCTION

BY

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Many recent studies have shown a relation between adrenal and thyroid functions, though its nature has not yet been defined. Depression of thyroid has been found when the adrenal is stimulated by A.C.T.H., by stress, or by adrenaline, or when cortisone is given; a few authors have reported benefit to the exophthalmos of Graves's disease from cortisone administration,[1 26] which others deny.[27 28 29] On the other hand, in Addison's disease thyroid function is apparently also low, as shown by basal metabolic rate (B.M.R.), by plasma-protein-bound iodine (P.B.I.), and by radioiodine uptake[1 25]; when such patients are given cortisone there is initially thyroid stimulation, but later thyroid depression.[25] In myxoedema are usually found low indices of adrenal function, low urinary 17-ketosteroids, low urinary reducing and formaldehydogenic steroids, and impaired eosinophil response to A.C.T.H.[1 4 5 6 24]; and partial correction of these abnormalities has sometimes been reported after treatment.[1 7] In thyrotoxicosis, involvement of the adrenal function has been long suspected, but its nature and its degree are still ill defined: 17-ketosteroid excretion is usually below normal in that condition[4 5 7]; the excretion of reducing steroids is said to be raised,[5 6] but low formaldehydogenic steroid output has been reported.[8] In animals, thyroxine administration has been found to induce a hypertrophy of the adrenal cortex.[9 10 12 13 17] Thiouracil or thyroidectomy is said by most authors to cause an atrophy of the adrenal cortex,[9 10 11 12 13 14 16 18 19 20] though a few have observed no change.[15 21 22]

This paper reports some measurements of adrenal function in thyrotoxic patients, both when untreated and after control by thiouracil. To assist in differentiating any effects due solely to the thiouracil, and not dependent on its effect on thyroid function, similar measurements have also been made in patients with primary myxoedema and in one normal subject at two or more levels of thyroid dosage.

Procedure

The thyrotoxic patients were first tested in hospital untreated, and then again when the thyrotoxic features had subsided—that is, after three to six weeks' treatment and while still receiving methylthiouracil. Five out of 10 patients received methylthiouracil, 200 mg. thrice daily; the remaining five had this dosage plus L-thyroxine, 0.45 mg. daily, and 10 mg. of potassium iodide daily. The pre- and post-treatment test procedures were planned to be an identical sequence, and were performed as follows: the patients were kept in hospital for two to three days; on the first morning, after a night's rest in hospital, the first 24 hours' collection of urine was started and the eosinophil depression test with A.C.T.H. carried out. The next morning the second 24 hours' collection of urine was started, and the eosinophil depression test with adrenaline performed.

The treated myxoedematous patients under full thyroid treatment were tested in the same way on what had been

established as the maintenance dose (thyroid, 1–4 g. (65–250 mg.) a day). They were again tested after three to six weeks' treatment with an increased thyroid dosage (usually doubled dosage).*

The untreated myxoedematous patients were also tested in the same way before institution of the treatment and after about three weeks on thyroxine, 0.1 mg. a day.

One normal subject was tested for three weeks before and after 500 mg. of "thyranon" daily, which led to symptoms of overdosage (tachycardia, sweating, nervousness, and some loss of weight). The B.M.R. rose from −1% to +30%, and the plasma cholesterol fell from 295 to 145 mg. per 100 ml.

The Patients

Nine of the 10 thyrotoxic cases (seven female, three male) were uncomplicated, typical, and clinically obvious; the other had thyrotoxic myopathy. The diagnosis was confirmed in all by the B.M.R. estimation, the urinary radioiodine excretion test, and the subsequent therapeutic response.

The nine treated myxoedema patients (eight female, one male) had been previously diagnosed as typical instances of severe primary myxoedema. At the time of the study they had been on a fixed and apparently optimal dosage of thyroxine for months and did not show any features of thyroid deficiency. The three untreated myxoedema patients were also typical instances of severe primary myxoedema.

Test Methods Used

Eosinophil Depression Test.—Carried out during the morning. Capillary blood was taken before and four hours after an injection of 25 mg. A.C.T.H. intramuscularly, and stained with a mixture of two-thirds of phloxine, and one-third of methylene blue diluted in 50% water and 50% propylene glycol. Each sample was counted eight times in Fuchs-Rosenthal cells. The patients fasted from the preceding evening, but the last cases were allowed to eat their breakfast after the A.C.T.H. injection and then fasted during the following four hours, the test being performed in the same condition before and after treatment. The Thorn adrenaline test was usually performed with 0.4 mg. of adrenaline subcutaneously the following day.

17-ketosteroids.—The method used resembles in all essentials that recently published by the M.R.C. Committee on Clinical Endocrinology.[30] Ethanolic potassium hydroxide stabilized with ascorbic acid[31] was used for the colour reaction; all readings of optical densities were made on the Hilger-Spekker absorptiometer, using Ilford 604 and 601 filters; the colour correction equation of Talbot *et al.*[32] was applied. Readings were made against a reagent blank. The standard used was an ethanolic solution of dehydro-*iso*-androsterone. At least two determinations were performed before and after treatment or modification of the treatment; but, whenever possible, more determinations were made if too much discrepancy between our creatinine figures made us suspect mistakes in collection of urine.

*Four patients went from thyroid 200 to 400 mg. (3 to 6 gr.) a day; three from thyroid 50 to 200 mg. a day; one from L-thyroxine 0.3 to 0.6 mg. a day; and one from thyroid 65 to 200 mg. (1 to 3 gr.) a day.

Results

Thyrotoxic Patients Tested Before and After Treatment with Methylthiouracil (see Table).—The pre-treatment 17-ketosteroids were low normal (from 14.9 to 2.48 mg.), but the post-treatment levels were significantly lower (T, 3.11; P, under 0.02). The pre-treatment eosinophil depression after A.C.T.H. was normal in nine out of ten, but after treatment the fall was diminished in seven out of nine, though not significantly so. No consistent change was discernible in the eosinophil depression test with adrenaline or in the levels of excretion of reducing steroid. It is worth pointing out that none of these patients except one showed any features of hypothyroidism at the second test.

Myxoedematous Patients, under Apparently Adequate Thyroid Treatment Tested Before and After an Increase in Thyroid Dosage (see Table).—In eight of the nine patients, judged clinically to be euthyroid, the initial 17-ketosteroid excretions were surprisingly low; the tests after the higher dosage gave a higher mean value which was not statistically significant. The initial eosinophil depression with A.C.T.H. was slight in three out of nine, and abnormally slight in one out of nine. On the higher dosage, in eight out of nine the eosinophil depression was greater, though again not statistically significant. The changes in eosinophil depression with adrenaline or in the excretion of reducing steroids were less consistent.

The clinical reactions of the nine patients to the raised dosage of thyroxine were variable, but six of them showed slight clinical features of hyperthyroidism. The B.M.R. increased slightly and the blood cholesterol fell in all but one.

Normal Subject Tested Before and After Large Doses of Thyroid.—The eosinophil depressions were slightly subnormal before treatment, and changed little after thyroid administration; both tests were repeated, with similar findings. The 17-ketosteroids rose after the thyroid administration.

Untreated Hypothyroid Patients Given Small Doses of Thyroxine (see Table).—The pre-treatment 17-ketosteroids were very low; after treatment slight rises were observed in two out of three patients. The pre-treatment eosinophil depression was below normal in two of the three patients; after treatment the eosinophil depression following A.C.T.H. was greater in all three.

Some Measures of Adrenal Function before and after Treatments Raising or Lowering Thyroid Function

Group	No. of Cases	Pretreatment Tests of Adrenal Function*				Change in these after Treatment† (Untreated—Treated)			
		Urinary 17-ketosteroids	Reducing Steroids	Eosinophil Depression 0–4 Hours		17-ketosteroids	Reducing Steroids	Eosinophil Depression 0–4 Hours	
				25 mg. A.C.T.H.	Adrenaline			25 mg. A.C.T.H.	Adrenaline
Thyrotoxicosis (before and after thiouracil)	10	7·8 (2·5–14·9)	4·19 (2·0–6·7)	63·2% (35–73%)	58·2% (36–77%)	−1·5‡ (fall in 9/10)	−0·5 (fall in 3/6)	−9·6 (fall in 7/9)	−1·3 (fall in 5/7)
Treated myxoedema (before and after extra thyroid)	9	4·5 (2·19–9·16)	4·10 (3·37–4·90)	54·5% (18–74%)	50·3% (20–64%)	+1·06 (rise in 6/9)	−0·5 (rise in 2/3)	+5·9 (rise in 8/9)	+4·3 (rise in 5/9)
Normal subject (before and after excess thyroid)	1	12·2	—	45%	11%	+4·95	—	+5	−9
Untreated myxoedema (before and after thyroid)	3	2·78 (1·15–4·40)	2·30	42% (26–54%)	40%	+1·05 (rise in 3/3)	+1 (rise in 1)	+19 (rise in 3/3)	+19 (rise in 1)

* Mean value and (range) shown. † Mean value and (number showing same trend) shown. ‡ Fall significant: T=3·11; P<0·02.

Discussion

In general, in this study there has been agreement between the 17-ketosteroid and A.C.T.H. eosinophil depression tests: where one has decreased the other has usually also done so. However, the adrenaline eosinophil depression test and particularly the urinary reducing steroid assay have

given variable and inconsistent results. All our reducing steroid results have been in the normal range,[28] and differences between two extracts of the same urine, or from day to day, have been commoner than as the result of treatment.

These tests suggest a fall in adrenal function when the thyrotoxic patients have been treated with methylthiouracil; the group is small, but the fall in 17-ketosteroids is significant and that in the A.C.T.H. eosinophil depression approaches significance in the small group. Further, when extra thyroid has been given, either to one normal or to nine myxoedema patients on a maintenance thyroid dosage, the opposite trend has usually been seen, though the changes are not significant in these small groups. Thus a lowering of raised thyroid function towards normal levels apparently causes an immediate decrease of adrenal function; and the change observed with the thyrotoxic patients is probably not merely a non-specific effect of the thiouracil. No such non-specific effect of thiouracil on the adrenal has been seen in animals, for with animal experiments it has been observed that the simultaneous administration of thyroxine prevents the adrenal atrophy seen with thiouracil.[9 13 19]

Our results with the few untreated myxoedema patients conform to those already published[1 7]—an increase of the lowered ketosteroid excretion and eosinophil depression. Thus our findings suggest that the immediate effect of raising thyroid function is to stimulate the adrenal cortex, and of lowering thyroid function to depress it. The low 17-ketosteroid excretion of thyrotoxicosis suggests that prolonged hyperthyroidism may have a different effect.

Summary

When 10 thyrotoxic patients were tested before and after control with thiouracil 17-ketosteroid secretion fell significantly and eosinophil depression after A.C.T.H. also fell, though not significantly.

When extra thyroid was given to nine myxoedema patients on a basic maintenance dosage and to one normal subject 17-ketosteroid excretion and eosinophil depression after A.C.T.H. rose, but not significantly.

In three untreated myxoedema patients 17-ketosteroid, and eosinophil depression after A.C.T.H., rose slightly following a few weeks of the initial thyroid dosage.

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A TUBERCULIN SURVEY IN STOKE-ON-TRENT

BY

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Tuberculin surveys of the population of the United Kingdom have been performed sporadically, usually on small and selected samples, over the last 30 years or more. Following a decision of the Ministry of Health authorizing the use of B.C.G. vaccine, the Medical Research Council organized a survey on a national scale to estimate the incidence of natural primary tuberculous infection in young people before the results of tuberculin-testing could be materially affected by the widespread use of B.C.G. vaccine.

The M.R.C. report (1952) describes in detail the organization of the survey, and Stoke-on-Trent was one of the 22 areas chosen for the test, which was carried out during the winter months of 1949–50. The present paper is an account of the findings in Stoke, and special attention has been given to the factors peculiar to the district which it is felt had a bearing upon the results obtained.

Present Survey

Stoke is an urban district some 10 miles by 4 in rural surroundings. The density of the population in 1949 was given as 13.05 persons per acre, but this figure is misleading, as a good deal of agricultural land is included in the city's boundary: in the 28 wards of the city it ranges between 4.82 and 37.15 per acre. The area covered by this survey and known collectively as the "Potteries," comprising the townships of Tunstall, Burslem, Hanley, Stoke, Fenton, and Longton, is highly industrialized. Housing is mainly of the small four-roomed terraced type, in which serious overcrowding is common. Among a variety of industries there are two in which the bulk of the population is engaged—pottery manufacture and coal-mining: in 1948, of a total population of 274,500, 56,000 were employed in the former and 15,000 in the latter. Both these occupations are attended by a serious although decreasing risk of pneumoconiosis, often complicated by pulmonary tuberculosis.

About half the people employed in the pottery industry are exposed to dust contamination, and of those who develop silicosis half may be expected sooner or later to become infected with tuberculosis. Approximately 750 cases of silicosis are existent at one time, and about 60 new cases are reported each year. Death from silico-tuberculosis is almost the normal termination of the disease in potters. Pneumoconiosis in miners is less often attended by superimposed open tuberculosis, and death from the combination of the two conditions is less common. There is thus a potential source of infection, especially in potters, which is peculiar to the district. It seemed that this was a factor

worthy of special notice in that the children of parents engaged in these two industries are apparently exposed to more than the average risk of tuberculous infection, as are also those who are themselves employed in them, and the results of an inquiry into this feature of the investigation are given below.

The survey was limited to persons between the ages of 5 and 20 years. Those of 5 to 14 years were all schoolchildren, but from 15 to 20 years they consisted of scholars, potters, and miners. In view of the exposure to silico-tuberculosis mentioned above, and with the approval of the M.R.C., no one otherwise employed was included.

Table I gives the number of persons concerned in the survey and their distribution by occupation and sex.

TABLE I.—*Numbers of Population Concerned in the Survey*

Age 5–20 Years	Scholars	Potters	Miners	Total
Total concerned	42,791	7,247	895	50,933
No. from which sample was drawn	9,729 (4,873 males, 4,856 females)	1,163 (326 males, 837 females)	254 (253 males, 1 female*)	11,146
No. tuberculin-tested	3,265 (1,602 males, 1,663 females)	495 (98 males, 397 females)	129 (128 males, 1 female*)	3,889

* A typist employed in a colliery office.

The 3,889 who received the tuberculin test represented 7.5% of the total population between the ages of 5 and 20 years, and 34.9% of the number from which the samples were drawn. The consent rate of just over one-third is much lower than the average reported by the M.R.C., and was due mainly to a lack of response among schoolchildren. There was a dearth of young persons in the pottery and mining industries; in the case of potters they were scattered through many factories, and in the time available it was possible to visit only some of the larger of these. A total of 40 schools (out of 178), 11 potteries, and three collieries were visited: these were well dispersed throughout the district, and were representative of the whole. It was considered that the sample of schoolchildren was quite random, and that the potters and miners were a fair cross-section of the population from which they were drawn. In some areas the value of the survey has been enhanced by submitting all positive reactors to examination by mass radiography. Unfortunately no unit was operating in Stoke at the time, and this procedure was not possible.

The method of tuberculin testing described in the M.R.C. report was adhered to in the present survey. All schoolchildren received the initial jelly test, and in negative reactors this was followed by an intradermal injection of 0.1 ml. of 1/100 dilution of old tuberculin (O.T.). The young potters and miners received an initial dose of 0.1 ml. of 1/10,000 dilution of O.T., and the non-reactors had a similar dose of 1/100 dilution. On several occasions it was noted when reading a second and positive test that the initial jelly test or intradermal test had reacted slightly, although previously negative. The impression was gained that had it been possible to read the jelly test at 96 hours instead of 72 a larger number of positive reactors to the jelly would have been recorded.

Results of the Tuberculin Tests

Table II shows the results of the tuberculin test for each year of age and for the sexes. It will be recalled that between the ages of 5 and 15 years the volunteers consisted of schoolchildren, and above this age young potters and miners were also included. The requirement of the M.R.C. that 250 persons should be tested in each year of age, divided as equally as possible between the sexes, was achieved through the range of 6 to 14 years, but there was a falling off in numbers from 15 years upwards. It will be noted that there was a steady increase in the number of positive reactors from 20.0% at 5 years to 77.2% at 18 years. The figure of 71.0% at 19 years is unreliable owing to the small number tested at that age. Fig. 1 expresses the results graphically and demonstrates the difference in positive reaction of the sexes: at no age is this difference significant.

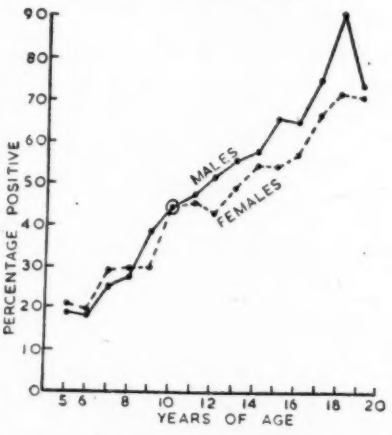

FIG. 1.—Percentage of positive reactors to tuberculin in Stoke-on-Trent.

The effect of the prevalence of silico-tuberculosis in the district upon the infection rate was also investigated. It seemed likely that the greatest risk of infection should exist among the children of those in whom the disease mainly occurs, and in Table III the results of the tuberculin test are presented in three groups according to the occupation of the parents—namely, potters' children, miners' children, and "others' children," the latter referring to the children of those otherwise employed. The numbers available for comparison were rather small, and the parents employed in potteries and mines amounted together to little more than half the remainder. Consequently the yearly infection rate varied greatly in the three groups, but in no group was this consistently higher than in the other two, and the

TABLE II.—*Number of Volunteers Tuberculin-tested, Showing Percentage of Positive Reactors**

Age in Years	Both Sexes				Males				Females			
	No. Tested	Reaction			No. Tested	Reaction			No. Tested	Reaction		
		+	−	%+		+	−	%+		+	−	%+
5	240	48	192	20·0	119	23	96	19·2	121	25	96	20·6
6	279	52	227	18·6	137	25	112	18·1	142	27	115	19·0
7	291	79	212	27·1	143	36	107	25·1	148	43	105	29·0
8	267	76	291	28·6	123	34	89	27·6	144	42	102	29·1
9	278	95	183	34·1	142	55	87	38·7	136	40	96	29·4
10	310	137	173	44·1	149	66	83	44·2	161	71	90	44·0
11	356	164	192	46·0	186	87	99	46·7	170	77	93	45·2
12	370	172	198	46·4	178	91	87	51·1	192	81	111	42·1
13	397	210	187	52·8	202	115	87	56·9	195	95	100	48·7
14	333	188	145	56·4	170	99	71	58·2	163	89	74	54·6
15	214	127	87	59·3	89	59	30	66·2	125	68	57	54·4
16	164	100	64	60·9	67	44	23	65·6	97	56	41	57·7
17	160	113	47	70·6	72	54	18	75·0	88	59	29	67·0
18	136	105	31	77·2	36	33	3	91·6	100	72	28	72·0
19	94	67	27	71·0	15	11	4	73·3	79	56	23	70·8
	3,889	1,733	2,156	44·5	1,828	832	996	45·5	2,061	901	1,160	43·7

* No person is included in this table who did not complete the test.

TABLE III.—*Percentage of Positive Reactors Subdivided According to Occupation of Parents*

Age in Years	Potters' Children				Miners' Children				"Others' Children"			
	Total Tested	+	−	%+	Total Tested	+	−	%+	Total Tested	+	−	%+
5	44	12	32	27·1	39	9	30	23·0	157	27	130	17·1
6	56	9	47	16·0	50	8	42	16·0	173	35	138	20·2
7	56	20	36	35·7	38	10	28	26·3	198	49	149	24·7
8	50	8	42	16·0	47	19	28	40·4	169	48	121	28·4
9	50	21	29	42·0	48	16	32	25·0	180	58	122	32·2
10	57	23	34	40·3	65	24	41	36·9	188	90	98	47·8
11	70	35	35	50·0	49	24	25	51·0	238	106	132	44·5
12	71	30	41	42·2	52	24	28	46·1	247	118	129	47·7
13	76	36	40	47·3	49	27	22	59·1	272	147	125	54·0
14	73	42	31	57·5	45	27	18	60·0	215	119	96	55·3
15	37	18	19	48·6	33	19	14	57·5	144	90	54	62·5
16	29	18	11	62·0	37	22	15	59·8	97	59	38	60·8
17	26	20	6	74·6	30	21	9	70·0	104	72	32	69·2
18	20	17	3	85·0	28	22	6	78·5	88	63	25	82·9
19	19	15	4	78·9	28	22	6	78·5	47	30	17	63·8
	734	324	410	44·0	638	294	344	46·0	2,517	1,111	1,406	44·1

average for all the volunteers in each ranged between 44.0% and 46.0%, a difference of 2.0% which is not statistically significant. The conclusion was reached that the occupation of the parent had no important effect upon the incidence of primary infection.

Effect of Environment upon the Results

It was felt that the effect of the conditions at school, workplace, or home should be inquired into, in so far as they might influence the chance of infection, and the schools and places of employment attended by the volunteers were graded according to the quality of their environment and social background. It was thought that where these were found to be of a high standard the risk of infection might be reduced, and the rate of primary infection correspondingly lower.

It was possible to divide the schools conveniently into three classes and nine groups according to their standard of hygiene and the age of the children attending them. Grade A schools were the best type, having modern buildings, and large and airy classrooms with no overcrowding. Facilities for sport were adequate, playing-fields often being attached; but in any case they were surrounded by open country or a residential area of at least the standard of a council house estate. Grade B schools failed to reach the standard of grade A schools in some respects. Sometimes the school itself was of a similar standard, but its environment was of low quality—slum or industrial area—and the means of proper recreation and allied facilities were lacking. Occasionally there was overcrowding. In the other cases the school was of inferior standard, but was well situated in surroundings equivalent to those of the grade A school. Grade C schools failed in every respect to reach the standard of the other two. They were always in old and dirty buildings, ill-lit and ill-ventilated, and were located in a slum or industrial area. There were no facilities for sport, and playgrounds were often unpaved. Overcrowding was frequent, and ablution and w.c. accommodation inadequate.

Broadly speaking, the standard of each school was in accordance with the home conditions of the scholars attending it, so that the better-cared-for children were found at the grade A schools and the more neglected ones at the schools of inferior grade. There were two exceptions to this observation in that at the two "high schools" visited, one for boys and the other for girls, a uniformly high degree of well-being and smartness was apparent, although the scholars were drawn from all types of district. No cases of gross malnutrition were seen at any school. Table IV gives details of the classification into the nine categories according to age and school attended, together with the percentage of primary infection, and it will be seen that the results for each age group did not differ widely at the three grades of schools. Although the difference is not significant it is of interest that at the grade C schools the lowest degree of infection was recorded instead of the highest, as might have been expected. It must, however, be inferred that the standard of school and home environment had no effect upon the frequency of tuberculous infection.

The 11 potteries visited were classified into three grades in a manner similar to the schools. One factory fell into grade A, seven into grade B, and three into grade C. The grade A factory was a modern well-lit and well-ventilated building in rural surroundings with excellent canteen and medical facilities. A welfare officer was employed and ample provision made for recreation. The grade B factories were in old buildings situated in highly industrialized areas. A welfare officer was employed, but no provision for sport or recreation was made. Canteen and medical facilities were adequate. Grade C factories were smaller buildings situated in highly industrialized areas, poorly equipped with canteen and medical facilities. No official welfare officer was employed, and there were no arrangements for sport or other recreation. In contrast with the schools, the employees at any factory were drawn from all parts of the district, and the factor of home environment was not related to the place of employment. Table V gives the number employed at each type of factory, and it will be seen that the infection rate of 70.7% at grade A potteries coincided with that at the grade C, whereas it was a little lower at grade B factories at 63.3%. The total number of volunteers in each grade was small, but the age group of 15–20 years was common to all three, and the number at each year of age in each grade was proportionate to the total for that grade. A reliable comparison may thus be made, and this indicated that the incidence of positive reactors among young potters was uninfluenced by any difference in their working conditions.

TABLE IV.—*Scholars Classified According to Age and Grade of School Attended*

Grade of School	Infants, 5–6 Years			Juniors, 7–10 Years			Seniors, 11–19 Years		
	No. Tested	No. +	%+	No. Tested	No. +	%+	No. Tested	No. +	%+
A	39	8	20·5	228	79	34·6	637	333	52·5
B	187	36	19·2	421	157	37·2	353	185	52·4
C	295	56	18·9	510	161	31·5	595	288	48·2
	521	100	19·1	1,159	397	34·2	1,585	806	50·8

TABLE V.—*Potters Classified According to Grade of Factory at Which Employed*

Grade A Factory			Grade B Factory			Grade C Factory		
No. Tested	No. +	%+	No. Tested	No. +	%+	No. Tested	No. +	%+
157	111	70·7	273	173	63·3	65	46	70·7

It was not possible to grade the three collieries visited, in a manner comparable to that adopted for the schools and potteries, and in any case the small number of miners concerned would have prevented any accurate conclusions being drawn.

Discussion

The M.R.C. report (1952) provides details of a standardized tuberculin survey in 22 representative areas of England and Wales on mainly unselected samples and has made it possible to compare the findings in different localities with accuracy. Perusal of the report will show that the results have been divided geographically into three areas, referred to as north urban, south urban, and rural areas, Stoke being included in the north urban area.

In Fig. 2 a curve indicating the yearly infection rate in Stoke has been added to the three representing the averages for the areas appearing in the M.R.C. report, and it is at once apparent that the incidence is substantially higher in Stoke at all ages than in the north or south urban areas, and at most ages is higher than in the rural area also. On further reference to the M.R.C. survey it is found that, of the 22 areas, the positive incidence in Stoke is the seventh highest at 5 to 6 years, the fifth at 9 to 10 years, the fourth at 13 to 14 years, and the second at 17 to 18 years.

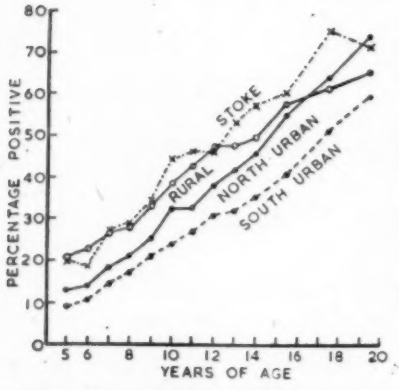

FIG. 2.—Percentage of positive reactors to tuberculin in the M.R.C. survey with the curve for Stoke-on-Trent superimposed.

It is of interest to speculate upon the reason for this high incidence of infection. The part played by milk, always suspect, may be ruled out in this instance, as the annual reports of the public health department for 1945–9 show that the proportion of tested samples of milk containing tubercle bacilli was negligible. The vital statistics recorded in these reports indicate high mortality and morbidity rates for tuberculosis. The mortality rate exceeded that for England and Wales by approximately 10 per 100,000 in 1945, rising to over 15 per 100,000 in 1949. The number of cases on the dispensary register rose from 1,671 in 1945 to 1,939 in 1949, and the number of known sputum-positive cases from 610 to 735 during the same period. The findings of a mass radiographic unit which began work in Stoke in 1952 confirm the high degree of morbidity. In the three months ending September 30, 8,448 persons had been *x*-rayed, revealing 6.8 cases of active tuberculosis per 1,000 examined. This is high compared with 6.3 per 1,000 for the Birmingham region, and the national figure of 3.5 per 1,000 quoted by the Ministry of Health in June, 1952. Among the Stoke examinees were 2,480 employed at three potteries, and 26 active cases were found, which was 10.5 per 1,000. Half the cases detected in earthenware factories were associated with pneumoconiosis. From this it seems reasonable to assume that infectious cases of silico-tuberculosis must form an important fraction of the whole.

It has already been shown that if the total number of volunteers is broken down into groups corresponding to those who were likely to be in close contact with cases of silico-tuberculosis and those who were not, there is no important difference in the proportion of positive reactors in each group. From this it would seem that all those taking part in the survey were exposed to much the same risk of infection, although this must have been greater in tuberculous households. One possible explanation of this is that the latter represent numerous small islands of infection scattered throughout the locality, and that the housing congestion combines with the "neighbourly" habits characteristic of the population of an industrial area to encourage exposure to open cases of tuberculosis. The high infection rate noted in schoolchildren may also be attributable to the same cause.

Summary

Stoke-on-Trent was one of 22 areas chosen by the Medical Research Council for inclusion in a national tuberculin survey in 1949, and 3,889 persons of 5–20 years of age were skin-tested.

Pneumoconiosis complicated by infective tuberculosis is prevalent among the many pottery workers (and to a less extent the coal-miners) in the district. The incidence of positive reactors among those whom it seemed were particularly exposed to infection from this source was no higher than in those who were not.

The quality of the environment of home, school, or workplace had no apparent effect upon the infection rate of the volunteers included in the survey.

The primary infection rate in Stoke was higher than the average for the other areas included in the M.R.C. survey, and it is suggested that this may be attributed to the high rate of morbidity from tuberculosis. The fact that no particular group of volunteers showed a greater incidence than the others was considered to be due to the close contact among all classes of persons which resulted from housing congestion and the custom of free social intercourse.

My thanks are due to the officials of the Departments of Health and Education of Stoke-on-Trent, and especially to the senior school medical officer and the members of her staff who assisted directly in the survey. I am grateful to the Federation of Pottery Manufacturers and the local division of the National Coal Board for their co-operation. I am also indebted to Dr. Peter Edwards, who made available the information on mass radiography and has kindly criticized this paper, and to Dr. A. C. Penman, with whom I was associated during the survey of schoolchildren and who has also offered valuable advice.

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In the third number of *Scientific Film Review* there are appraisals of ten medical films: "Anaemia" (E. R. Squibb and Sons) intended for students, general practitioners, and medical societies; "Electromyography of Postural Muscles—Leg and Thigh" (Guy's Hospital) intended for students and postgraduates of physiology and specialists in physical medicine; "Hay Fever" (St. Mary's Hospital Medical College) intended for medical societies and lay people interested in the subject; "The Human Blood Fluke" (Wellcome Film Unit) intended for undergraduate and postgraduate students of tropical medicine and hygiene; "Mitral Valvotomy" (Guy's Hospital) intended for undergraduate and postgraduate students of surgery; "Movements of the Ureter" (Wellcome Film Unit) intended for undergraduates and postgraduates of physiology; "Prevention of Cross-infection—Airborne Infection" (Central Film Library) intended for student nurses, and valuable for medical auxiliaries in contact with hospital patients; "Principles of Penicillin Therapy" (E. R. Squibb and Sons) for undergraduate and graduate students of medicine; "Pronestyl Hydrochloride" (E. R. Squibb and Sons) for anaesthetists and cardiologists; "Rheumatism and Rehabilitation" (Dr. Bach and Edward Langley) for physiotherapists and nurses. The *Review* is obtainable from the British Film Institute, 164, Shaftesbury Avenue, London, W.C.2. Annual subscription 5s., single copies 1s. 6d.

A CASE OF COR TRILOCULARE BIATRIATUM WITH SURVIVAL TO ADULT LIFE

BY

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Cor triloculare biatriatum is an uncommon anomaly, and survival into adult life is exceptional. In Abbott's (1936) analysis of 1,000 cases of congenital heart disease the condition occurred 13 times as a primary defect and in a further 14 complicating other abnormalities. In her series the age at death ranged from infancy to 35 years, the mean being 7¼ years. Included among these are four patients who lived to be 21 years or more. Other cases reaching adolescence or adult life are those of Favorite (1934) with survival to 18 years, Drey *et al.* (1938) 14 years, Carns *et al.* (1941) 44 years, Mehta and Hewlett (1945) 56 years, and the famous case of Holmes (1824) in which death occurred at 21. Mann (1907) described a case of his own surviving to 35 and quotes three others living to 22, 24, and 39. Messeloff and Weaver (1951) reported a case of transposition of the great vessels with a ventricular septal defect and survival to 38 years. In the nine cases reported from the Mayo Clinic, the oldest was only eight years (Rogers and Edwards, 1951). Other cases described, with death in childhood, are those of Kornblum (1935), Taussig (1939), Glendy *et al.* (1944), Greenberg (1949), Brown (1950), Richman (1950), and Keizer (1952).

A large ventricular septal defect may give rise to a heart that is functionally triloculate but anatomically four-chambered. Apart from this cause the condition may arise as the result of an extremely early arrest in the development of the heart. A single ventricle remains with, as a rule, a rudimentary outlet chamber representing the bulbus cordis (Taussig, 1947). A quite different malformation results from tricuspid atresia and absence or defective development of the right ventricle. Cases have also been described with mitral atresia and a rudimentary left ventricle. This type of case is functionally biloculate.

Taussig (1939) described three types of cor triloculare biatriatum associated with a rudimentary outlet chamber: (1) both systemic and pulmonary circulations arise from the outlet chamber; (2) the aorta arises from the common ventricle, and the pulmonary artery from the outlet chamber; and (3) the aorta arises from the outlet chamber, and the pulmonary artery from the ventricle. The last is the more common variant, and is usually associated with transposition of the vessels. Associated abnormalities are common, the most frequently recorded being an atrial septal defect.

A Case Report

A man aged 24 was admitted to the Weymouth and District Hospital on September 24, 1951, following a haematemesis. He gave a history of cyanosis since birth. He had always been dyspnoeic on exertion and had never worked. He had had intermittent epigastric pain for a number of years, coming on about two hours after meals. This was accompanied on occasions by vomiting; it was not relieved by food, and alkalis had not been tried. For about two and a half weeks before admission he had noticed that he was passing black stools. During this time he had become increasingly breathless. For three days he had had some vomiting, and on the day of admission this had contained altered blood.

Examination showed him to be of normal stature but poor development. He was pale, cyanosed, and dyspnoeic. There was gross clubbing of the fingers and toes. The pulse was 100, regular. The blood pressure was 140/80. The jugular venous pressure was not raised and no giant "a" waves were seen. The heart was greatly enlarged to the left, with a heaving quality at the apex and movement of the ribs. There was pulsation in the region of the "right ventricular outflow tract" and pulmonary valve closure was palpable. A systolic thrill was felt, maximal in the second left interspace. On auscultation there was a presystolic triple rhythm; the second sound was split, with accentuation of the pulmonary element. A systolic murmur was audible over most of the heart, maximal in the second left interspace. It was not heard between the scapulae. There was a blowing diastolic murmur audible down the left border of the sternum. The chest and abdomen showed no significant abnormalities.

The haemoglobin on admission was 64% (8.6 g.); red cells 3,750,000; colour index 0.85. This level was maintained for several days, later starting to drop. Despite repeated blood transfusions his general condition deteriorated, the haematemesis recurred, and he died on October 5.

A tentative clinical diagnosis of Eisenmenger's complex was made with regard to the cardiac abnormality.

Post-mortem Report

The heart was large (750 g.) and showed what appeared to be considerable right-sided hypertrophy. The main vessels were transposed, the aorta arising to the right and anteriorly, with the pulmonary artery behind and to the left. There was no evidence of a persistent ductus arteriosus. The arch of the aorta reached the level of the third thoracic vertebra at its highest point, and was firmly adherent to the vertebral column. This resulted in a sharp downward bend instead of the normal smooth curve. The thoracic and abdominal aorta were left-sided.

On opening the heart it was found to have a single ventricle and two atria. The foramen ovale was patent. The tricuspid and mitral valves were normal. The pulmonary artery was dilated, and admitted three fingers; it arose from the common ventricle. The aorta was a small thin-walled vessel admitting only one finger; this arose from a rudimentary outlet chamber, partially walled off from the ventricle by a ridge of myocardium 3.5 cm. thick. Elsewhere the ventricular wall measured 2 to 2.5 cm. The coronary arteries took origin from the aorta.

The stomach contained a few ounces of clotted blood. There were multiple superficial erosions. One slightly deeper area of erosion was seen on the lesser curve, 5 cm. from the pylorus. These appeared to have been oozing blood recently. The small and large intestine contained altered blood. The liver was normal. The spleen was congested. There was slight oedema at the lung bases. Other organs were normal.

The histology of the stomach showed gross dilatation of the mucosal and submucosal venules. Some of these could be traced to the surface, where erosion of the mucous membrane had caused them to bleed.

Discussion

Brown (1950) stated that when the pulmonary artery arises from the rudimentary outlet chamber cyanosis tends to be severe. When, however, it arises from the common ventricle cyanosis is absent or at most slight. The presence

of early and pronounced cyanosis in our case is thus of interest. In Abbott's series cyanosis was reported in 11 out of 13 cases; in only three was it severe, and in two it was terminal. In the nine cases of Rogers and Edwards (1951) cyanosis was mild or terminal in five cases, in three it was moderate, and in one it appeared at the age of 7 months—the child dying when 10 months old. Clubbing was reported in only one of Abbott's cases.

A systolic murmur was recorded in five of Abbott's series, and in one further case a continuous murmur was found. None had a thrill. A systolic murmur was present in all of the eight cases from the Mayo Clinic (Rogers and Edwards, 1951) in which the physical findings were recorded. In two of these it was accompanied by a thrill. In no case was a diastolic murmur found. Glendy *et al.* (1944) found an apical mid-diastolic murmur, which they regarded as due to blood flow through a relatively stenotic mitral valve into a dilated ventricle. Carns *et al.* (1941) and Greenberg (1949) reported similar diastolic murmurs to that found in our patient. Favorite (1934) recorded a diastolic murmur at the aortic area. We considered that the murmurs which we heard were most probably due to increased blood flow through the pulmonary artery, with some degree of regurgitation.

In our case the palpable pulmonary outflow, the split second sound with accentuation of the pulmonary element, the systolic thrill, and the systolic and blowing diastolic murmurs all suggested a diagnosis of Eisenmenger's complex. The diagnosis of cor triloculare biatriatum is one of considerable difficulty. Several authors have described particular radiological contours, but these appear to be far from constant. The electrocardiogram may show right or left ventricular preponderance (Rogers and Edwards, 1951). Catheter studies and angiocardiography are unlikely to distinguish the condition from Eisenmenger's complex. Miller *et al.* (1950) have diagnosed the abnormality in life, in a child of 5½. In their case only one vessel was seen leaving the base of the heart, the blood supply to the lungs arising from the descending aorta. They remarked that the "presence of only mild cyanosis at rest, the fluoroscopic contour of the heart, and the absence of murmurs are important signs in the clinical diagnosis of a single ventricle." However, all these points are open to doubt.

Summary

A case of cor triloculare biatriatum is described, with survival to 24 years.

The types of cor triloculare biatriatum are briefly described.

The findings in a number of other reported cases are discussed.

We wish to thank Dr. E. B. Jarrett, Dr. P. Hughes, and Dr. T. V. Cooper for permission to publish this case.

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Medical Memorandum

Perforation of Tuberculous Ulcer of Small Intestine

Perforation of the small intestine from any cause does not commonly occur, and perforation of a tuberculous ulcer is rare. Only a few original papers on this subject have appeared in the literature in the past fifteen years, recording a small number of cases all of which occurred outside this country. This makes the present case of interest.

Case Report

A boy aged 14 was admitted to the Glasgow Royal Infirmary with a history that eight months previously he had experienced lassitude, lack of interest in his surroundings, and anorexia. *X*-ray examination of the chest at that time had shown the typical appearances of miliary tuberculosis; no clinical signs of tuberculosis had been found in the chest, abdomen, or central nervous system. He had been treated in hospital, and had received streptomycin.

Three and a half hours before his present admission he had suddenly had severe central abdominal pain, which had later moved to the right iliac fossa. He also complained of pain in the tip of the right shoulder. There was vomiting but no diarrhoea. On examination he was seen to be a small, pale, and toxic-looking boy. His temperature was 101.6° F. (38.7° C.) and pulse 160. The tongue was furred. There was generalized tenderness and rigidity in the abdomen, maximal in the right iliac fossa.

Operation.—A right paramedian incision was made. The peritoneal cavity contained thin yellow pus, and the appendix was inflamed as part of a general peritonitis, but was not the cause of it. There were numerous tuberculous ulcers lying transversely across the terminal ileum, tending to constrict the bowel: one ulcer ½ in. (1.3 cm.) from the ileo-caecal valve showed a perforation 4 mm. in diameter which was leaking ileal contents. The perforation was closed, the peritoneal cavity cleaned, the appendix removed, and the wound sutured.

The patient made a good recovery and was discharged on the twenty-third day after operation to another hospital to continue treatment for tuberculosis.

Comment

The rarity of perforation in tuberculous ulceration of the small intestine is probably in part due to the relatively slow pathological process (compared, for example, with enteric fever). This permits time for adequate fibrous tissue formation in the base of the ulcers, so that stricture formation is a commoner complication.

Ameuille and Duperrat (1937) published observations on 30 cases of perforated ulcerative enteritis combined with pulmonary tuberculosis. Ameuille and Chevalier (1939) recorded one case with multiple perforations. Galavotti and Diletti (1937) described a double perforation in one case, and Lamberti (1941) and d'Ovidio and Bellingi (1943) published comments on cases of perforated tuberculous ulcers (numbers unknown). Black (1943) and Dussaut and di Laudo (1944) have each described one case of single perforation.

The case under discussion resembled fulminating obstructive appendicitis in the clinical picture, but the abrupt onset of symptoms and the rapid progress of the toxic signs combined with the previous history of miliary tuberculosis gave a good pre-operative hint of the true pathology.

I am indebted to Mr. A. M. Clark for permission to publish these notes.

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Reviews

SURGERY OF PARKINSON'S DISEASE

Parkinson's Disease and its Surgical Treatment. By Leslie Oliver, F.R.C.S. (Pp. 88; illustrated. 12s. 6d.) London: H. K. Lewis. 1953.

In this short monograph the possibilities of surgery in the relief of parkinsonism are discussed, with particular emphasis on spinal pyramidotomy and its various modifications. The aim of surgical treatment is to relieve tremor, and the author is surely right when he emphasizes that attempts to do this when disabilities resulting from other features of the complaint are paramount can only worsen the patient's state. The book is based on the examination of over 1,000 patients with parkinsonism, of whom 300 were admitted to hospital for full study and 93 finally selected for operation. It is clear from the results of lateral pyramidotomy (Putnam) in 70 patients that this operation should be limited to cases of unilateral tremor; even here only half the cases are benefited, and recovery from the post-operative hemiplegia is incomplete in some. Oliver's extension of this operation to include section of the whole lateral column is encouraging in the relief of tremor it affords. Out of fourteen cases it was substantially relieved in all, but at the cost of contralateral analgesia and a variable degree of homolateral hemiparesis, although from the case summaries presented it is impressive to note the degree of motor recovery that does take place. This indeed would seem to be the crux of the problem; when unilateral tremor is of such a degree to be of itself grossly disabling, then the relief to be obtained by operation may override the added operative effects. The tremor must be long-standing, strictly unilateral, and unaccompanied by other gross manifestations of the disease. These provisos restrict the operation to a very small proportion of sufferers, and, as Oliver concludes, the findings reported in this book will dispel many extravagant claims which have been made for surgery in this complaint, even though it may give relief in selected cases. The later follow-up results of these cases will be awaited with interest. At the end of the book the various intracranial procedures which are also under trial for this complaint are summarized.

WALPOLE LEWIN.

AMPULLA OF VATER

The Roentgen Aspects of the Papilla and Ampulla of Vater. By Professor Maxwell H. Poppel, M.D., F.A.C.R., Harold G. Jacobson, M.D., F.A.C.R., and Robert W. Smith, M.D. (Pp. 195; 150 illustrations. 61s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1953.

This short but expensive monograph will interest a wider public than radiologists: gastro-enterologists, abdominal surgeons, and anatomists will all find it instructive. About one-third of the work is devoted to various aspects of anatomy. Professor Boydon has given advice on embryology and anatomy and his work has been extensively quoted and illustrated.

The authors show how surprisingly often the major papilla can be seen radiologically as a routine, without the aid of special spot films, if sufficient radiographs are taken. In 500 unselected upper gastro-intestinal studies they were able to demonstrate the major papilla on at least one film in 48.8% of cases.

The main object of their thesis is the radiological diagnosis of "diseases of the Vaterian segment." Very appropriately they prefix their observations on pathological changes by discussing and illustrating the radiological appearances, not only of the normal but also of the congenitally large papilla and heterotopic pancreatic tissue. Thence they go on to describe fifteen personal cases of malignancy of the Vaterian segment—carcinoma of the ampulla of Vater and of the supra-ampullary intraduodenal duct segment—all demonstrated radiologically. It is a fine collection. The radiological differential diagnosis from carcinoma of the pancreatic head or duodenum is discussed in a later section. Other very rare lesions such as benign tumours of the papilla are mentioned.

The authors have devoted themselves to a very limited and specialized field, but anyone interested will find this little book most useful.

J. W. D. BULL.

BIOCHEMISTRY AND METABOLISM

Biochemistry and Human Metabolism. By Burnham S. Walker, M.D., Ph.D., William C. Boyd, Ph.D., and Isaac Asimov, Ph.D. Foreword by John T. Edsall, M.D. (Pp. 812; 21 figures. 68s. 6d.) London: Baillière, Tindall and Cox. 1952.

This book is intended primarily for medical students, and much organic chemistry has been omitted so that more attention can be given to the relationship of fundamental biochemistry to the clinical applications of the subject. But where the chemistry is needed it is included, and the reader who wishes to understand what 17-ketosteroids are and how they are related to steroid hormones finds sufficient but not too much for his purpose.

The book is divided into six parts. Part I—"Structure"—is on proteins, tissue chemistry, blood, and the anaemias. Part II—"Control"—covers enzymes and hormones. Part III—"Growth"—is on nucleoproteins, cancer, and reproduction and heredity. Part IV—"Metabolism"—includes nine chapters on the expected subjects, all lucidly written. Part V—"Pathology"—covers vitamins, vitamin-deficiency diseases, and infection. And Part VI consists in appendices on colloids, isotopes, thermodynamics, and acids and bases.

The chapter on reproduction and heredity in Part III includes a valuable section on genetics, covering among other topics the subject of blood groups and their biochemical significance. The interpenetration of biochemistry and genetics, foreshadowed in Garrod's classical work on inborn errors of metabolism, has been one of the exciting developments of the past two decades, but it is unfortunately true that the medical man still knows too little about genetics and even less about the relationship of biochemistry to the subject. Here he will find a useful introduction to it.

The index is excellent, and the book is printed and produced in the admirable fashion one expects of the Williams and Wilkins Company. But the binding, at least of the volume in the reviewer's hands, appears to be a little less rugged than might be needed in a book that will undoubtedly be often referred to by those who are fortunate enough to possess it.

F. G. YOUNG.

RADIOLOGY OF THE SKELETON

Roentgen Diagnostics. By H. R. Schinz, W. E. Baensch, E. Friedl, and E. Uehlinger. First American edition (based on the fifth Swiss edition); English translation arranged and edited by Professor James T. Case, M.D., D.M.R.E. Volume II; skeleton (part 2). (Pp. 1,190; 1,500 illustrations. £15.) London: William Heinemann. 1952.

This is the second volume of a monumental work and itself consists of 1,150 pages of text with 1,500 illustrations. It now renders accessible to English readers a German work which has gradually grown to encyclopaedic dimensions and to which we in Britain have no parallel. It is difficult in a short review to convey any idea of its content or of its scope.

The volume opens with a discussion of primary bone tumours, based on their radioscopic appearances but giving at the same time an adequate account of their pathology. In each group the radiographs are accompanied by photomicrographs and diagrams which show at a glance the common sites of occurrence. Metastatic tumours are described in a similar manner, a clear picture being given of their occurrence and distribution. There follows a chapter on skeletal malformations into which is compressed much information on the development of the skeleton and the origin of some of its most perplexing deformities. Sections

follow on disturbances of growth and their relation to vitamins and hormones, giving information briefly but with remarkable clarity and completeness on subjects of absorbing interest and recent development.

The next section is headed "Joint Injuries," but it contains much information on the anatomy and physiology of the joints and on methods of their examination. It is indeed a revelation of how much can be learnt from the study of radiographs taken under controlled conditions. It includes a brilliant study of the knee-joint, illustrated by contrast radiographs and photographs of cartilages removed by operation. Injury is taken in a liberal sense, for the section includes a full discussion of infective arthritis, degenerations, and hereditary joint disease.

The vertebral column is well described and beautifully illustrated with full details of the abnormalities which may occur and of the methods of *x*-ray examination, a special section being devoted to myelography and the many problems which it poses, especially in the localization of tumours affecting the spinal cord.

The section on the skull and its contents is most impressive both for the beauty of the plates and for the explanatory diagrams accompanying them; these add greatly to their value. This is especially so in the chapter on ventriculography and in the really superb account of angiography of the cerebral vessels, a triumph of combined technique. A later chapter on angiography in the limbs stresses the perfection to which this technique has been brought. The whole book is packed with original ideas, but at the very end is a chapter on the differential diagnosis of skeletal diseases in which their distribution and characteristics are brought at once to the eye in a series of simple line sketches which both impress the memory and tell more in a few lines than one might extract from many pages.

This is a work of quite outstanding importance and of the highest scientific value. It is superbly produced, and as the reader studies its pages he ceases to regard the price as high and comes to wonder how so much of practical value could have been gathered into so attractive and clear a form. It is indeed a book for the close study of all who are interested in the bony framework of human beings.

HENRY SOUTTAR.

FAMOUS NEUROLOGISTS

The Founders of Neurology: One Hundred and Thirty-three Biographical Sketches prepared for the Fourth International Neurological Congress in Paris by 84 Authors. Edited by Webb Haymaker, M.D. With the bibliographical and editorial assistance of Karl A. Baer. (Pp. 479; illustrated. £3 15s. 6d.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1953.

This book is a mine of interesting historical and neurological information. We dipped into it here and there until the whole 133 biographies had been read, and found it a rich feast. A debt of thanks is due to the medical department of the United States Army and to the editor who prepared and presented this tribute to the Fourth International Neurological Congress in 1949. Every neurologist and most physicians will probably need to have this book on their shelves.

Each biography has a photograph of the subject treated, and most of the 84 authors insert some incident which makes the person they are describing come to life and stand before the reader. We leave the reader to discover for himself the name of the Saxon who had such little love for socialism that when at necropsy he looked at the brain of a prominent socialist he was impelled to remark: "My! What disharmonic convolutions!" We believe there are few neurologists who could say which physician in charge of a mad king was knocked on the head and then drowned by his patient, who thereafter waded deeper into the water and drowned himself; or which neuro-anatomist wrote his own obituary notice, ending with the words, "God bless America"; or recall which neuro-anatomist used to sing all the time he was working in his laboratory.

We liked the story told of Augustus Waller, the famous son of a famous father, who, when his father's name was mentioned, used to say, "I am *the* Wallerian degeneration!" And that of the casual Meynert, who, when greeted by a comrade with the remark, "A very stormy day," retorted, "I have not yet had time to think about it."

The names of many famous British neurologists are included, not only Ferrier, Gowers, Hughlings Jackson, and Horsley but those of more recent times such as Kinnier Wilson, Adie, Stansfield Collier, and George Riddoch. It is related that Henry Head one day eagerly rushed up to Hughlings Jackson to describe some new observation he had made, only to be put off with the remark, "Don't bother me now, Head, I'm making some observations on my own migraine." We could quote many other vivid pen-pictures of these great neurologists, but we think the reader should find them for himself. In any case he will find intense interest in scrutinizing the reproductions of photographs, many of them taken in the early days of photography, and in trying to read the character of those who are thus portrayed. A fascinating book.

ZACHARY COPE.

PREVENTION OF BILHARZIA

The Snail Hosts of Bilharzia in Africa: Their Occurrence and Destruction. By A. Mozley, D.Sc., Ph.D., F.R.S.Ed. (Pp. 78; illustrated. 9s.) London: H. K. Lewis and Co. 1951.

A Background for the Prevention of Bilharzia. By A. Mozley, D.Sc., Ph.D., F.R.S.Ed. (Pp. 71; illustrated. 9s.) London: H. K. Lewis and Co. 1953.

The author states in the preface to the first of these volumes that it is intended for laymen. For this reason it has been written in very simple terms and at times in a rather colloquial manner. Most of the space is given to descriptions of habitats of the snails, both natural and artificial, to the factors which contribute to the spread of infection, and to methods of control. The author briefly describes the life history of the worms and includes a chapter on the recognition of dangerous species of snails, but no method is given by which snails can be proved to be infected. One-quarter of the space is devoted to methods of snail destruction, the principal method advocated being the use of copper sulphate, which is stated to be the only molluscicide which meets all essential requirements. The more recent molluscicides are barely named and are dismissed without mentioning the very encouraging reports of their field trials. The author's solution of the bilharzia problem appears to be the provision of safe water supplies (bore-holes, etc.) and the use of copper sulphate. These are practicable methods for concentrated populations and commercial undertakings, but are too expensive for innumerable African villages. Insufficient emphasis is laid on such cheap methods as impounding springs to supply safe domestic water, and health education is dismissed as ineffective. This book will prove of little value to those concerned with the control of bilharzia, because it is oversimplified. It might be of some use in the instruction of junior African sanitary personnel.

The second book is concerned only with African bilharziasis, though this qualification does not appear in the title, which might also, but incorrectly, lead one to expect concrete information about control measures. But preventive methods are referred to in general terms only and the subject is not treated systematically. There is much discussion of snail ecology, and suggestions are made for employing naturalistic control measures which have not yet been proved effective. The main interest is in the snails, the factors affecting their occurrences, the types of surface water in which they are found, and in the plants and animals living in association with them. A number of contradictory statements are made and there are important omissions. The use of colloquial expressions may encourage reading of the book by laymen, but will irritate workers accustomed to scientific literature. This book will not satisfy those concerned with the bilharzia problem in Africa, and it is too vague and discursive for those wishing to learn about the subject. The illustrations are excellent.

T. H. DAVEY.

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ECONOMICAL PRESCRIBING

Exasperated by the latest attempt of the Ministry of Health to encourage what it conceives to be economical prescribing, a correspondent asks this week in the *Supplement* (p. 178): "Is it not time we made a stand against all this nonsense?" No doubt he is echoing the thoughts of general practitioners up and down the country. The occasion of this protest is some advice recently sent (in a pamphlet) by the Ministry to general practitioners in the Health Service. It shows the cost of *National Formulary* preparations, and compares the cost of some commonly prescribed proprietaries with that of their so-called *B.P.* or *B.P.C.* equivalents. After the scathing remarks made from time to time by Ministers of Health and their political supporters on the large sums said to have been wasted on proprietary preparations, it may come as a surprise to the reader of this booklet to learn that many of them cost less than the non-proprietary equivalent. The Ministry has listed 244 proprietaries and 124 non-proprietaries for comparison of cost. The difference between these two—namely, 120—is the number of proprietary drugs commonly prescribed for which there is no official equivalent. They all seem to be respectable drugs judged by those standards that are being set up in Whitehall, and no doubt the Ministry cannot cavil at their being prescribed. Of the remaining 124 proprietary drugs with listed equivalents, 48 are cheaper than the official preparation and 9 cost the same. There are thus 67 proprietaries left which cost more than the equivalent, and probably many of these owe part of their higher cost to being dispensed in a more pleasing vehicle—even perhaps a more efficacious one—than the official equivalent. Apart from the light it throws on the economical prices charged for most proprietary drugs—though there are a few curious exceptions—this booklet will not be of much interest to doctors, and to that great majority of doctors who are careful prescribers there are already indications that it is a cause of resentment.

Even so, the nation's drug bill is a matter of concern to taxpayers. Some figures available for England and Wales show that in 1950 the cost was £34.8m., and it rose to £43.8m. in 1952 (before deduction of the charges of 1s.). The proportion of the cost attributed to proprietaries was 32% in 1950 and 44.5% in 1952. It is against this background that we have to look at the labours of the Joint Committee on Prescribing, whose classification of proprietary medicines was issued (as a pamphlet) to all doctors in the Health Service last July, together with a letter from the Chief Medical Officer of the Ministry of Health. One of the suggestions he made to reduce prescribing costs was that doctors should not prescribe preparations in categories 5 and 6 of that list. Drugs in category 6 are simply drugs in category 5 compounded with drugs in the approved category 4, so that it is inclusion of a drug in category 5 that is intended to make its prescription difficult to justify. Some of the drugs thus placed beyond the pale in this category are certainly unlikely to commend themselves to many doctors. But the category apparently includes two other groups of drugs—namely, drugs whose value is not yet proved, and drugs with dangerous side-effects. We thus have a committee with the backing of the Ministry telling doctors that they had better not prescribe certain drugs unless their action has been proved to some unspecified body's satisfaction, and attempting to deprive doctors of the responsibility of judging whether, in a particular case, the benefits of a drug outweigh the danger of side-effects from it. These are clinical judgments that have nothing to do with the economics of prescribing. While the committee that drew up these categories emphasized in an earlier report[1] that "responsibility for prescribing should rest solely with the practitioner," the Chief Medical Officer of the Ministry, endorsing this guidance, adds that a general practitioner may "be called on to justify the cost of his prescribing to his colleagues on the local medical committee." All this is coming perilously near to banning certain drugs at the behest of the Ministry. It is not surprising that the Minister has recently told doctors—albeit with grim humour—that they take far too much notice of instructions from the Ministry, for, he added, "healthy independence and a certain amount of healthy disobedience would be a very good sign."[2]

When these affairs were discussed in the General Medical Services Committee of the B.M.A. last

[1] *Second Interim Report of the Joint Committee on Prescribing.* H.M.S.O. 1950. See also *British Medical Journal Supplement*, July 8, 1950, p. 24.
[2] *Daily Telegraph*, October 15.
[3] See p. 176 of *Supplement* for report.

week[3] members showed a lively anxiety about them. Fully aware of the need for economy—and indeed that economical prescribing is good doctoring—many speakers expressed the impatience that is widespread among general practitioners at these misguided endeavours to cut costs by virtually blacklisting certain preparations. Some check on prescribing is an inevitable corollary of a State service, and the one most favoured seems to be by areal averages. Any doctor greatly exceeding the average for his area in prescribing costs is required to justify his prescribing to the local medical committee. At that stage, and no earlier, the committee might want to hear some information about what drugs the doctor is prescribing, and it may be trusted to use intelligently the powers statutorily put upon it to curb any extravagance. Nor is it the prescribing of proprietaries as against non-proprietaries that is the real problem here. As some members of the G.M.S. Committee emphasized, it is in the quantities prescribed, whether of official or proprietary drugs, that there is room for economy. Fewer pills and smaller packets on each prescription might well cut the cost effectively. In prescribing, as in many other affairs, the dangers of restriction are far greater than the dangers of liberty.

HEIGHTS AND WEIGHTS OF SCHOOLCHILDREN

The heights and weights of their children are a matter of great interest to parents, yet medical students learn little, if anything, about what has now become a considerable subject. Measurements of heights and weights of children have been recorded for some seventy years, and average heights and weights at given ages have tended to increase throughout that time. The latest values repeatedly set up new records.[1] This secular trend has been remarkably persistent, and there are no signs yet that it is even approaching a limit. Nevertheless it has not been constant.[2] It was probably reversed during the first world war and perhaps slowed down during the second.

Elsewhere in this issue Dr. E. M. B. Clements has assembled a variety of data collected in London, Birmingham, and Glasgow from about 1880 to 1947. From the figures it appears that average children living in 1947 were about 3 in. (7.6 cm.) taller and 8 lb. (3.6 kg.) heavier than children of corresponding age living in 1910 or earlier. The change is smaller for the younger and greater for the older children. It is also relatively greater for the poorer than for the wealthier. These increases are equivalent to 18 months' to 2 years' growth, and indicate an acceleration of about 15% in forty years. The data are fragmentary, but appear to indicate that the rate of change has varied considerably over this period. A more reliable picture is obtained from the data for a single locality. Ewan[3] has graphed the heights and weights of Glasgow schoolchildren from 1910 to 1951 at yearly intervals, apart from a short break during the first world war and a single year (1940) during the second. Each point corresponds to the average measurements of some 6,000 boys or girls in one age group and thus has a very small standard error. The upward trend of the secular change is clearly visible, and so are the slowings associated with the depressions in the early 1920s and early 1930s. It is also evident that the gradient has scarcely been affected by the recent war.

Using London 1938 figures[4] as a standard, Weir[2] has drawn up tables giving age corresponding to height and age corresponding to weight. These greatly facilitate the comparison of data without standardizing for age, and lead to two indices of growth—a rate for growth in height and a rate for growth in weight. The indices express growth rate as a percentage of the London 1938 values and make it much easier to compare different school populations. So far only the tables for boys' measurements have been issued. The growth rate indices for London in 1905–12 were 88.3 for height, 86.6 for weight. This is in comparison with 1938, the chosen standard year, when they were taken to be 100. By 1949 they had risen to 103.9 and 102.2. In 1950 they were 105.1 and 103.1. The Birmingham values in 1947 were 103.0 and 101.8, and were thus very similar to those of London. The Glasgow values, on the other hand, have consistently lagged behind the London figures. In 1938 they were 93.8 and 93.7. Since then they have steadily crept up: in 1949, 99.1 and 98.5; in 1950, 99.3 and 98.9; in 1951, 99.8 and 99.1; and in 1952, 100.2 and 99.3. Not only are the Glasgow indices lower than those

[1] Morant, G. M., *Brit. med. Bull.*, 1951, **7**, 316.
[2] Weir, J. B. de V., *Brit. J. Nutr.*, 1952, **6**, 19.
[3] Ewan, J., *Report on the Medical Inspection and Treatment of School Children.* Glasgow: Education Health Service, Public Health Department, Corporation of Glasgow. 1952.
[4] Menzies, F., *Report by the School Medical Officer on the Average Heights and Weights of Elementary School Children in the County of London in 1938.* London: London County Council. 1940.
[5] Morant, G. M., *Biometrika*, 1948, **35**, 368.
[6] —— *Proc. roy. Soc. B*, 1950, **137**, 443.
[7] Kemsley, W. F. F., *Ann. Eugen. (Camb.)*, 1950, **15**, 161.
[8] Durnin, J. V. G. A., and Weir, J. B. de V., *British Medical Journal*, 1952, **1**, 1006.
[9] Daley, A., *Report on the Heights and Weights of School Pupils in the County of London.* London: London County Council. 1950.

for London, they are lower than those for divisions 4 and 5, the two poorest of London's nine health divisions. In 1949 divisions 4 and 5 together had indices of 102.1 and 101.6. We do not know whether this difference is due to geographical or socio-economic factors or to something else, but a comparison of adult heights may give the answer; for, as Morant[1] has pointed out, while growth rates vary within limits in response to living conditions, average height reached at maturity is presumably genetically determined.

Children of to-day are, on average, growing considerably faster than their ancestors were two generations ago. They are not necessarily different in physique, and there is little if any increase in the adult stature reached at maturity.[5-8] A corollary is that they stop growing at an earlier age. Thus Morant finds that the maximum stature attained by an individual is now reached by about the age of 20 years instead of 27 years as it was around 1880. Individuals vary, and the slow growers compensate to some extent by growing for a longer period than the fast growers. The increased rates of growth amount to 15% or more. To see these marked changes in proper perspective, they may be compared with the variations within the school population at any one time. Figures are available for London children in 1949,[9] and they show that the secular change in about 40 years amounts to one standard deviation of the corresponding measurement, height or weight. The improvement is most marked among the most retarded, so that the scatter is diminishing. It is hard to realize that in the middle age groups there is a range of some 20 in. (50 cm.) in height and 100 lb. (45 kg.) in weight. Putting it another way, we may say that children aged 10 years may be as small as an average child of 6 years or as big as an average child of 14 years. Some are growing much faster than others, and there seems to be no biological reason why the present secular change in an upwards direction should not continue at least to the end of the century.

ENZYMES AND THEIR ACTIVITIES

A catalyst is a substance which when present in very small quantities will enhance the speed and completion of a chemical reaction. Enzymes are the catalysts of the chemical reactions taking place in living tissue. One summary of their properties reads as follows: "Proteins are no doubt formed by enzyme action, and since enzymes are proteins it follows that enzymes are formed by enzymes, and this is probably the main reason why living matter is always found to be formed from living matter."[1] More crudely, enzymes might be described as the motor units of living matter. Outside the body enzymes play a vital part in the production of beer and bread and cheese; inside the body they are able to modify these and a variety of other foods that take our fancy into the correct fuel to enable the cells of our tissues to carry out their many and varied functions. In a recent issue of the *British Medical Bulletin*[2] some aspects of enzyme research are described in a series of interesting articles.

Enzymes are extremely numerous and of diverse and often highly specialized function, and they frequently operate in cycles so that a series of chemical reactions follow one another in quick but fixed succession. Just as most mammals have a similar respiratory mechanism in which air is taken in and oxygen carried in combination with haemoglobin, so do many cells have similar mechanisms for respiration which usually involve the transfer of hydrogen through a series of compounds while energy is produced, and its final combination with oxygen and excretion as water. Some properties of the pigments that do this—the cytochromes—are discussed by Professor Keilin, to whom biochemistry is indebted for the recognition of their importance and function. Professor Krebs discusses the transformation of energy in living matter, and, despite the rather forbidding tables and chains of reaction that illustrate it, this article should be read. It emphasizes the uniformity rather than the diversity of these processes, thus lending hope to the less well informed reader that one day he may be able to understand much more.

Despite these common pathways, each organ must also have different enzyme systems for its special function. We should not feel flattered if we thought that those enzymes suitable for maintaining bone would also suffice for our cerebral activities. The liver is clearly called upon to do work very different from that of the heart. Sir Rudolf Peters reviews some of the factors that disturb the pyruvate oxidase system vital in brain metabolism and discusses interference by specific substances such as fluoroacetate, of which an account recently appeared in our pages.[3] That enzymes may be upset or inhibited by substances closely resembling those they normally act upon was clearly shown twenty-five years ago by Quastel. He discusses the way that drugs interfere with enzyme systems, and a study of this may well throw light on how drugs and poisons upset the organism. In this article Quastel suggests the way

[1] Dixon, M., *Multi-enzyme Systems*, London, 1949.
[2] *Brit. med. Bull.*, 1953, **9**, 85-168.
[3] Peters, R. A., *British Medical Journal*, 1952, **2**, 1165.
[4] Mellanby, E., ibid., 1946, **2**, 885.

in which the product of agene and flour gluten which produced fits in dogs[4] might interfere with an enzyme system. Woods first developed the idea of competition for enzymes to explain the antibacterial action of sulphonamides, and so provided a rational approach to chemotherapy. He has continued to study the metabolism of bacteria, because it is clear that in many respects it resembles the metabolism of the body cells. The same vitamins essential for mammalian well-being are also growth factors for bacteria because they are essential to important enzyme reactions. Woods has studied folic acid, which the animal requires for the satisfactory multiplication of the blood cells. It is an essential factor in the growth of bacteria, and its function can be studied in detail more readily in the test-tube than in the bone marrow. So fascinating has the study of enzymes become that we find an article by a professor of physical chemistry venturing into fields which might almost be said to border on the political aspects of genetics. Professor Hinshelwood by his work has shown the value to biology of a fresh view of things brought by someone trained in other disciplines than biological research.

The cells and the organs have their special enzymes, and so too there are enzymes of a more general distribution which may be related to the function of the body as a whole. The cholinesterases hydrolyse acetylcholine in the test-tube and presumably also in the body at points where acetylcholine functions. The properties and distribution of these enzymes are described, but the full story of their function remains to be told. The existence of an enzyme able to inactivate adrenaline suggested that it too might be distributed in places where the rapid destruction of adrenaline might be advantageous. However, the distribution of amine oxidase makes it difficult yet to ascribe an important function to it. The enzymes hydrolysing phosphate esters—the phosphatases—have been studied extensively for many years. The existence of simple laboratory methods for their estimation has no doubt been responsible for the wide study of their presence and activity in human blood. The transfer of phosphate is probably one of the most important steps in the metabolism of the tissues, but an empirical association of blood phosphatase activity with certain diseases cannot yet be linked in any way with what we know of these more intimate cellular reactions.

Wide and diverse as are the articles in this excellent symposium, they leave many aspects of the fascinating field almost undescribed. The extensive use of radioactive isotopes in enzyme work has led to the substantiation of what were previously well-founded conjectures. Other workers are studying the components of the cells by differential centrifugation and finding that enzymes or groups of enzymes are associated with the small particulate cell structures such as the mitochondria. We cannot do better than conclude with the final words of Peters in his introduction to the volume: "But the best still lies ahead with its bright promise that the global efforts to apply chemistry and biochemistry to enzymes will prove powerful enough to establish a therapy based upon logical knowledge of the biochemistry of the cell and so to transform much that constitutes pathology to-day."

CLOT RETENTION

The fear of blood clot collecting in the bladder and preventing micturition has played a significant part in the development and adoption of many operations on the bladder and prostate. When bleeding from the upper urinary tract or from the bladder is mild or moderate the dilution of the blood by the urine is often sufficient to prevent clotting, or the clot forms only at the site of bleeding and is passed in small, irregular fragments. If the bleeding is more rapid, but the bladder is competent and the outlet free, then the blood is passed as soft clots, which may or may not be moulded to some part of the urinary tract. But if the outlet of the bladder is obstructed and if the blood collects in some relatively insensitive part of it, such as on the posterior wall when the foot of the bed is raised, or while the patient is comatose, it may become firmly organized. Then it cannot be passed, but will obstruct the passage of urine. The increasing distension of the bladder with urine, and the presence of the clot, cause a constant desire to get rid of the foreign body. The result is bladder spasm amounting often to severe pain and a degree of shock out of all proportion to the loss of blood. The presence of this foreign body in the bladder does nothing to prevent further bleeding; on the contrary it interferes with the normal mechanism for stopping haemorrhage in a cavity, that of contracting down on the bleeding point. It is therefore essential to remove the clot.

If the bleeding is pre-operative and is probably coming from the prostate gland, it has long been the accepted teaching that cystostomy not only allows the clot to be removed but will stop the bleeding. If the clot has arisen from post-operative bleeding from the bladder or prostatic cavity, then it is probable that the bladder has been closed and drainage is by catheter. The age and general condition of the patient once clot retention has been established make reopening of the bladder a major surgical measure, so that evacuation through the catheter is most desirable. In most cases gentle irrigation and suction with a Wardill glass syringe or a Thompson

[1] Smith, E. P., Jr., *et al.*, *Surg. Gynec. Obstet.*, 1953, **96**, 171.
[2] Tillett, W. S., and Garner, R. L., *J. exp. Med.*, 1933, **58**, 485.
[3] —— and Sherry, S., *J. clin. Invest.*, 1949, **28**, 173.

metal syringe will evacuate all the clot. If the catheter is too small or collapses with suction, then a Tiemann–Marion catheter of as large a size as can be passed under a local analgesic will evacuate all but the hardest clot. The routine irrigation with 5% sodium citrate solution in order to prevent clot forming is less popular now than formerly. Once clot is thoroughly organized it may resist evacuation even through a Bigelow evacuator, which will require a general anaesthetic.

Previously the only effective method of liquefying such clot was a solution of pepsin in glycerin, which was often painful and increased the shock. But recently Smith, Toulson, and Rever[1] developed a different method by applying the work of Tillett and Garner[2] and Tillett and Sherry[3] on fibrinolytic enzymes of the haemolytic streptococci. They injected these enzymes—streptokinase and streptodornase—first into the bladders of normal dogs without producing any gross reaction, and secondly into the bladders of dogs in which areas of mucosa had been resected in order to cause bleeding. No further bleeding was caused. They then used it in eleven patients, in three of whom the bleeding came from the upper urinary tract and in eight from the prostatic cavity after prostatectomy. In the post-prostatectomy cases a solution of 100,000 units of streptokinase and 25,000 units of streptodornase, dissolved in 20 ml. of normal saline, was injected into the bladder and allowed to remain for fifteen minutes. During this time traction was applied to the inflated Foley's catheter in order to prevent the solution from reaching the prostatic cavity. The bladder was then washed out with sterile water. In the case of bleeding from the upper urinary tract the same quantity of enzyme was dissolved in a similar amount of saline, but introduced from an irrigating apparatus, so that it could be regularly repeated. It was allowed to remain in the bladder for the same length of time. The results are reported as being extremely gratifying. This method of treating clot retention appears to be a satisfactory way of treating a condition which has so long caused much anxiety.

MEDRESCO HEARING-AIDS

The Ministry of Health has recently announced the issue of a new Mark III Medresco hearing-aid with increased power and smaller batteries, and earlier in the year, after extensive tests and field trials, an aid with a bone-conduction receiver was produced. Thus there is now available under the National Health Service a comprehensive range of hearing-aids sufficient to meet the needs of nearly all hard-of-hearing people capable of being helped by an aid. In the past there has been some criticism of the size and weight of the batteries, but large batteries have the advantage of long life and comparative cheapness. Fortunately it has been possible to reduce the size and weight of the batteries for the new Mark III, and Medresco users will welcome them. Those severely deafened patients who have always preferred the original Mark I aid should find the additional power of the new aid most helpful. While the Medresco aid with bone-conduction receiver will be needed for those few deaf people (less than 1% of the total) who can hear speech better by means of bone conduction, another small group (probably not more than 5% of the total) will prefer it because ear discharge or a sensitive meatus makes an insert receiver undesirable.

It may be some time before all who wish to use either of these two new aids can be supplied with them. At present the Mark III aid should ordinarily be first supplied to children, while the increased rate of battery consumption by the bone-conduction aid means that it will be prudent to issue it only on medical grounds and not for aesthetic reasons.

Since the first Medresco hearing-aids were issued in August, 1948, more than 320,000 deaf or hard-of-hearing people have received them through over 50 hearing-aid distribution centres. All those using small insert receivers fitting into the external auditory meatus—most of the users—have been encouraged to obtain individually moulded rather than ready-made inserts. The shape and size of the external meatus vary so widely that it is not easy to find a really close fit with a ready-made insert, and the advantages of a perfectly fitting insert far outweigh the trouble entailed in taking the impression and having the insert made and finally fitted. In fact the extra visit to the distribution centre to get the individual insert enables the patient to receive additional instruction in the use of the aid.

Not long ago a columnist in one of the daily papers wrote that, to him, one of the notable features of New York was the large number of people in the street who were wearing hearing-aids. The same might also be said of London now, and the time seems to be coming when a hearing-aid will attract no more attention than a pair of spectacles, for it is certainly much less obtrusive. But it cannot be denied that a hearing-aid is still more of a nuisance to the user than a pair of spectacles. It has to be concealed in the clothes, batteries have to be changed, and leads are apt to break; and occasionally one of the valves, or the switch, or one of the condensers goes out of order, even when treated with care. Like a pair of spectacles, it can be broken by careless handling, though it is surprising how robust these aids are. At one time it was thought that three years would be the working life of an aid, but most Medresco aids in use for three years or more are still going strong.

Since 1948 the popularity of these aids has noticeably extended. Formerly few deaf children wore aids, but now a visit to any special deaf school reveals that most of the pupils, even though they may have but a tiny remnant of hearing, cheerfully wear them; even children of 3 and 4 wear them in a kind of harness, and object to being parted from them. The new smaller batteries will be an advantage for both children and the aged, and there are hopes of eventually producing an even smaller aid with contained batteries for children. To the aged deaf, these aids have often proved a blessing, though they are the hardest group to help with an aid. There is no doubt that the benefit extended to so many deaf people by the Medresco aid is ample return for the trouble and cost of providing a hearing-aid service on a national scale.

CLINICAL PATHOLOGY IN GENERAL PRACTICE

VENEPUNCTURE

BY

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There are nine and sixty ways of constructing tribal lays,
And-every-single-one-of-them-is-right !—KIPLING.

As venepuncture is so commonly performed, it is probably the subject of more likes and dislikes and individual variations in technique than any other minor medical procedure. No author can do more than state one series of preferences, many of which may be anathema to those practising a different approach. What follows, therefore, is clearly open to limitless minor variations and cannot please everyone.

Venepuncture in the adult, where the vein to be entered is usually large and visible, is quite different from that in the infant, where the chosen vein is not seen but must be entered by the observation of anatomical landmarks. The two will be considered separately; in both it will be assumed that there is available a sterile syringe with airtight plunger, together with an unblunted needle not smaller than size B.W.G. Smaller needles are not materially less painful for the patient, and withdrawing of blood through them is more difficult and more liable to yield a haemolysed specimen.

As bacteria may interfere with so many tests the aim of every venepuncture should be to obtain a sterile sample of blood to be transferred into a sterile container.

After the hands have been thoroughly scrubbed and dried the instruments are examined. Whatever the size of the patient an essential preliminary to any venepuncture is to assemble the syringe and ensure that the plunger moves freely and the needle has not become blocked. The needle should be placed on the syringe nozzle with sterile forceps—if it was not in position before sterilization. No part of the fingers should touch the needle or the surface of the plunger, either at this stage or when the vein is being entered. In choosing a syringe one larger than apparently necessary is always to be preferred to one the size of the blood sample needed, as so often air bubbles replace much of the space which should contain blood. A 10 ml. syringe is suitable for most purposes. It should be ensured that the cover of the container into which the blood is to be put is free so that it can be removed with one hand while the other expels the blood into the bottle or tube (this is particularly important with screw-capped bottles).

Adults

Both for ease and convenience the antecubital fossa veins are nearly always used (see Fig. 1), with the arm lying on a table of convenient height. Either the central or lateral veins are used; in spite of the way the lateral accessory cephalic vein stands out the cephalic or median cubital veins are bigger and easier to penetrate. The lateral vein is more mobile and therefore more likely to be pushed aside, and incidentally it is more painful to have punctured.

1. Inspect and palpate the antecubital fossa and select the vein to be used. If necessary compress the upper arm with the free hand to make the veins stand out; if the patient "makes a fist" a few times this will help.

2. Sterilize the skin of the antecubital fossa with whatever antiseptic is preferred. Weak iodine solution, cetrimide, spirit, or ether are commonly used; a coloured antiseptic is useful, as the painted area can be seen.

3. Obstruct the venous return by compressing the upper arm. This can be done with a piece of rubber tubing, tied as in Fig. 1 for quick release, with a sphygmomanometer cuff inflated to a pressure of 90–100 mm. Hg, or by getting the patient to grip his upper arm with his free hand so that the veins are compressed beneath the belly of the biceps against the humerus. This can be demonstrated when selecting the vein, and is often advantageous in the nervous patient as it takes his mind off the coming prick and makes him feel he is being useful.

4. Set the arm supine on the table and resterilize the skin.

5. Get the patient to make a few more fists, then tell him to keep quite still and enter the selected vein. The bevel of the needle should face the skin, to minimize the risk of transfixing the vein. The vein may be approached directly through the skin over it or by penetrating the skin at the side of it and then attempting to enter the vein from its side. The first procedure is much the easier, but large and simple-looking veins are sometimes pushed aside by the needle.

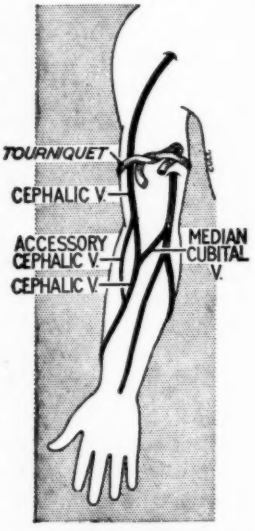

FIG. 1.—Veins of the arm, with quick-release tourniquet in position.

6. Make slight suction on the syringe with the free hand when it is thought that the needle is in the vein. If no blood enters the syringe push it gently forward in the line of the vein, keeping up slight suction. If about two-thirds of the needle have gone into the arm and no blood has been obtained it is legitimate with the free hand to palpate the skin to feel where the needle point is. Then, making gentle suction again, slowly withdraw the needle to but not out of the skin, stopping immediately, of course, should blood be obtained. If still unsuccessful the process should be repeated, more than once if necessary, until the blood is obtained.

If swelling in the antecubital fossa, blue discoloration of the skin, or oozing of blood round the needle should appear, indicating haematoma formation, the pressure on the upper arm is released immediately, a swab with antiseptic on it is placed gently over the needle, the needle is withdrawn sharply—at the same time pressing the swab down firmly—and the patient is told to bend his arm double tightly. Haematomas are obviously caused by damage to the vein, usually by exploring too deeply and through its deep wall.

7. When blood is entering the syringe freely, slacken off the pressure on the upper arm. In fat arms, where the veins can be palpated but not seen, and sometimes when they cannot even be palpated, it may be necessary to maintain the obstructive pressure until the syringe is full. If blood starts to enter the syringe and then stops it can usually be got flowing again by moving the point of the needle slightly; often merely elevating the point is effective. Too great suction should not be made on the plunger, as this tends to drag air into the barrel, giving a smaller yield of blood than is required.

8. When the requisite blood is in the syringe, make sure that all pressure is released from the upper arm, hold a swab over the site of puncture, withdraw the needle sharply, at the same time pressing the swab down firmly. Tell the patient to bend his arm double and keep still. Hold the syringe with the needle slightly upwards; if it is held pointing downwards blood may drip out, while if held too high the plunger has been known to fall out of a full syringe.

9. Deal with the blood sample, distributing it into the appropriate containers.

10. Wash out the syringe and needle with water, and dismantle the syringe.

11. By this time any bleeding from the patient's arm should have stopped. Straighten his arm gently, at the same time keep-

ing light pressure on the swab for a few further seconds. Remove the swab and bathe the antecubital fossa with more antiseptic. Any tendency to ooze can be controlled by further pressure for a minute or two, or the arm may be held vertically for half a minute while moderate pressure is maintained on the puncture.

12. Nothing further should be necessary, although some like to put a small piece of adhesive plaster over the puncture.

The above is essentially a "no-touch" technique, and, provided the needle and the patient's sterilized skin are not touched, should yield a sterile blood sample. Nothing can be deprecated more than a guiding finger lying along the needle, a practice all too often seen. The technique is perfectly simple to carry out single-handed, although more efficacious hand-washing drill can be practised if there is someone to assist by passing swabs and holding blood containers.

Adult venepuncture may be unsuccessful in the most expert hands for many reasons. The two commonest are either simply failure to enter the vein or damage to the vein with haematoma formation. In the former case the arm should be re-sterilized and another vein attempted. When a haematoma has been caused no further obstructive pressure should be made on the arm, which would lead to further blood extravasation, and after ensuring by firm pressure that any bleeding and oozing has stopped an attempt should be made on the other arm.

Children

By the age of 5 most children have veins well enough developed for the above technique to be used, and often as young as 3 a successful venepuncture can be performed. As distinct from an adult, who usually wants to get the business over and is therefore co-operative, children will generally struggle, and assistance is imperative if an effective puncture is to be carried out. Even when the arm is skilfully held above and below the elbow it is amazing how much movement the average child can still achieve. The operator must remember to be most flexible and prepared to allow his hand, the syringe, and particularly the point of the needle to move with the wriggling that the child's arm may produce. Movement is minimized if the arm is abducted and externally rotated so that the back of the wrist lies flat on the couch. The hand of the assistant round the biceps acts as a tourniquet, but often with smaller arms the assistant's second hand at the child's wrist seems enormously in the way. A rehearsal without the syringe will usually enable the operator and assistant to dispose themselves most conveniently.

Infants

From birth to the age of about 3 years visible or palpable veins cannot be expected, and some other approach must be made. The most popular, particularly where quantities of blood up to 10 ml. are required, is the internal jugular vein, while the external jugular, the femoral, or scalp veins are sometimes used. The technical preliminaries regarding apparatus and sterilization are exactly the same as for adult venepuncture.

Internal Jugular Puncture.—The essence of this simple and safe procedure is in the position of the baby. It is first wrapped tightly in a blanket which comes up to the shoulders and retains the baby's arms at its sides. The baby is then held on its back with its head just overhanging the edge of a couch or cot. The head is rotated away from the side to be punctured, so that the sternomastoid muscle is put on the stretch. After sterilizing the skin, the operator inserts the needle at the posterior border of the sternomastoid, halfway between the mastoid process and the sternal notch (Fig. 2). Then, maintaining gentle suction on the plunger, the needle is pushed slowly beneath the muscle in a direction at right angles to the long axis of the baby. The underside of the sternomastoid is easily felt with the tip of the needle, and the aim is to keep as closely under the muscle as possible. In the majority of cases the blood will enter the syringe almost immediately and the required amount can be withdrawn. The position of the internal jugular vein varies from child to child; it may be necessary to push the needle across the neck as far as three-quarters of an inch (2 cm.) or more before blood is obtained. If no blood flows the needle is slowly withdrawn, maintaining suction all the time, until the tip of the needle can be seen under the skin at the point of entry. The traverse beneath the sternomastoid can then be repeated until the vein is entered. After blood is withdrawn moderate pressure with a sterile swab is maintained over the site of puncture for about half a minute. If the attempt at venepuncture is unsuccessful on one side of the neck the same procedure should be carried out on the other. The secret of the technique seems to be the full extension and rotation of the child's head, and blood is got much more readily from a crying child than from one which none of this handling causes to cry. A variation of this method of internal jugular puncture is to enter the skin at the mid-point of the posterior border of the sternomastoid, the needle then being directed towards the sternal notch. This oblique approach has nothing to commend it over the direct approach, while anatomically it is potentially more dangerous.

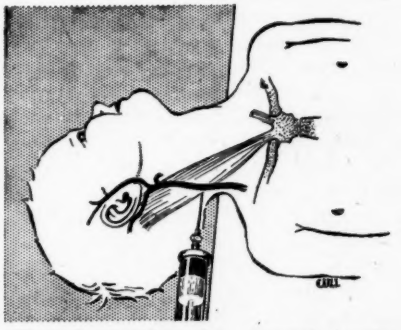

Fig. 2.—Position for internal jugular puncture, showing the course of the external jugular vein.

External Jugular Puncture.—The external jugular vein runs obviously and temptingly across the sternomastoid (Fig. 2), and puncture of it is often unsuccessfully attempted. The reason is that the vein is relatively unfixed, and is so mobile that it is more likely to be pushed aside than penetrated by the needle. On occasions the vein can be successfully punctured, and it makes no difference whether the direction of the needle is towards the head or the heart.

Femoral Vein.—This lies on the medial side of the femoral artery, and can be entered just distal to the inguinal ligament. The baby is held flat on its back with a sandbag under its buttocks, and after the position of the vein has been ascertained by palpation of the artery the needle is either directed towards the heart or else thrust vertically into and through the vein, blood being sucked into the syringe after the point of the needle has been slightly withdrawn. Large amounts of blood may be got from the femoral vein, which has been used with increasing frequency in recent years (Fig. 3).

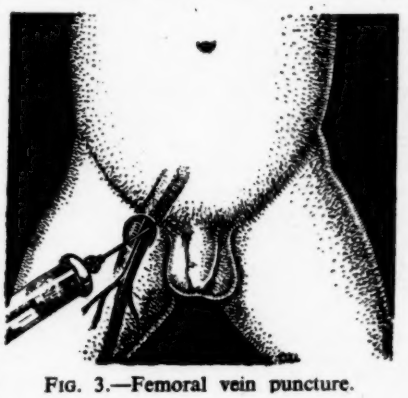

Fig. 3.—Femoral vein puncture.

Scalp Veins.—Small amounts of blood may be obtained from these. The wrapped baby is held with its head on one side, while digital pressure is made in front of the pinna of the ear. With the scalp over the temple and above the ear shaved a choice of three or four small veins will be seen lying between the top of the head and the front of the ear. They are brought into greater prominence if percussed lightly. The importance of the scalp veins is not so much as a source of blood as a channel through which small intravenous injections may be given, particularly in the newborn.

It will be appreciated that when it is desirable that all of a substance should be given intravenously with none in the surrounding tissues none of the other methods of venepuncture in infants is satisfactory, as the exact position of the needle point cannot be seen. The infant's scalp veins can be seen, withdrawal of a little blood will ensure that the needle is truly in the vein, and as the veins are so superficial any of the injection fluid not entering the vein can be seen and the injection stopped at once.

Fontanelle puncture was formerly much used in infants, a special short needle with a short bevel and a guard being introduced through the posterior angle of the anterior fontanelle into the superior sagittal sinus. This method is not without risk, and now that other techniques have been perfected it should no longer be used.

Cord Blood.—This should not be forgotten as a simple and ready source of blood where the necessity for blood examination is likely to arise immediately after birth. It is easy to collect, and equally easy to discard should it not be wanted.

Heel Prick.—Lastly, in spite of the available methods of venepuncture in infants there are occasional cases where all efforts to get venous blood are unsuccessful. In these, and in cases where not more than 1 ml. of blood is required and sterility is not important, the possibilities of the heel prick should not be forgotten. While it is capillary and not venous blood which is so obtained the great majority of clinical laboratory tests can be performed on it, especially as so many biochemical tests are now being adapted to micro-methods. The heel should be thoroughly warmed first and the skin sterilized; then, being held so that the first finger and thumb of the left hand can milk the soft tissues (Fig. 4), the point of the heel is sharply jabbed with a needle with a cutting edge; the edge faces towards the toes, and as the needle is withdrawn it is dragged slightly distally to enlarge the opening in the skin. By this means a free flow of blood may be established, which is allowed to drop into a bijou bottle (where any necessary anticoagulant can be mixed with the blood by agitation) or collected into a Lyon's tube (a small glass tube carrying a hole near the top through which air can escape as the blood runs in) or Wright's capsule.

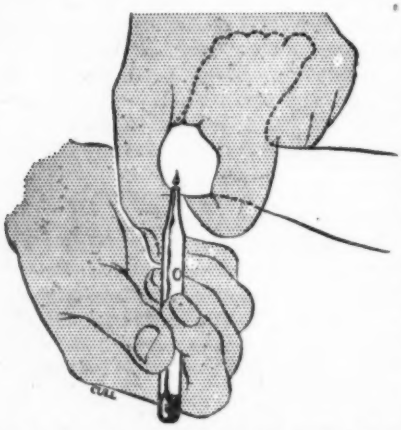

FIG. 4.—Milking blood from the heel into a Lyon's tube.

The methods outlined above are all well tried and have been found adequate for their purpose. Successful venepuncture calls for no comment, but failure to obtain blood can be the most exasperating and humiliating experience. Seeking to analyse the reasons for success or failure, there can be little doubt that the main essentials for success are a sharp needle, gentleness, and, above all, not being in too much of a hurry.

Next article on Clinical Pathology.—"Pleural, Pericardial, and Peritoneal Tap," by Dr. Thomas Parkinson.

Refresher Course Book.—The first collection of articles in the Refresher Course for General Practitioners (fully revised) are available as a book containing 55 chapters, price 25s. Copies can be obtained either direct from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or from booksellers.

THE DUKE OF EDINBURGH

HONORARY F.R.C.S.

The Duke of Edinburgh visited the Royal College of Surgeons on October 20 to receive the Honorary Fellowship of the College. He was welcomed by the President (Sir Cecil Wakeley) and the Vice-Presidents.

Sir Cecil Wakeley said that every Fellow, Member, and Diplomate of the College shared in their pleasure in conferring on the Duke the greatest honour within their power. The Royal College was closely associated with the Royal Family, and only two years ago the Queen, then the Princess Elizabeth, had been made an Honorary Fellow. He went on to mention the Duke's interest in many branches of science, and said that, over and above the deep affection with which they regarded the Queen and his Royal Highness, they looked upon them both as the personification of a new spirit in their midst—a spirit of confidence and new endeavour. The Senior Vice-President (Sir Reginald Watson-Jones) then presented the Duke for admission to the Honorary Fellowship and the President admitted him.

The Duke of Edinburgh said that he had been interested in a remark by Sir Cecil Wakeley to the effect that surgery was both an art and a science. He did not pretend to know anything about surgery, but, looking at it purely from the layman's point of view, he hoped that the practitioner artist and the scientific researcher would always continue to work in close harmony. He could not help thinking what a bad thing it would be if, with the increasing complexity in all branches of scientific work, the two were to grow apart. He spoke of his great pleasure in following in the footsteps of so many distinguished members of the Royal Family. With them he shared a common admiration for surgeons and surgery, and (they would forgive him for saying) a common ignorance of this noble craft. He added that he had a special satisfaction in becoming an honorary surgeon, because he felt that if ever he came under the surgeon's knife the surgeon would remember that he was operating on a colleague.

THE NEW ACADEMIC YEAR

WESTMINSTER MEDICAL SCHOOL

The inaugural address at Westminster Medical School was given on October 12 at Church House by Lord Radcliffe, Lord of Appeal. Mr. H. M. Clowes, chairman of the school council, presided, and those present included the Mayor of Westminster, the Directors-General of the three armed Services, and Lord Nathan, chairman of the board of governors of Westminster Hospital.

The Inquiring Mind

LORD RADCLIFFE said that he had been reading the reports of the recent First World Conference on Medical Education, and had been impressed by the frequency with which it was stated that the person training in medicine and surgery should not become so immersed in his subject as to forgo the claims of general education and culture. This was a precept not only for those intending a medical career but also for those who were entering other professions, such as engineering. A wider general education must support their specialized knowledge. The leaders of industry were asking for men not merely qualified in their special branches of study but with a wider general background. This was one of the problems of the age. Times had changed since the recognized curriculum could cover all general education. It was quite right for the young person to wish to be a specialist. His wits were alive, he realized the fascination of his particular subject, and dived head foremost into it with all the enthusiasm he could command. It was a good thing to become a man with a craft; it gave him self-confidence and a footing in life which he would otherwise fail to find. The days of universal knowledge

were past. Christopher Wren was said to have been one of the last of men possessed of such knowledge. But with the accumulation of specialized learning had come about the breaking up of the old curriculum on which general culture was founded.

What was to be done about it? They were all agreed that they would be better men if they had a wider range of education. "Twenty Questions" on the B.B.C., brains trusts, and even courses of lectures would not provide the answer. He would offer only one piece of advice to students—that they should keep their curiosity alive. Curiosity was one of the great factors in promoting civilization.

"When you become masters of your craft you will be sustained to the end if you always keep alive an inquiring mind. Let your curiosity take you into the paths that appeal to you. Be curious and do not take things for granted. Then you will find that life is continually opening before you, with new fields upon which your mind can dwell."

A vote of thanks to Lord Radcliffe was accorded on the motion of Dr. AUBREY GOODWIN, seconded by Mr. R. COYTE.

Reports of Societies

MANCHESTER MEDICAL SOCIETY

At a meeting of the Section of Pathology held on October 14, Dr. J. F. WILKINSON opened a symposium on "Transfusion Problems." He said that, while the transfusion of blood and blood products was often a life-saving measure, it could also be wasteful, unnecessary, and even dangerous. The decision to transfuse a patient and the type and quantity of the product to be used—whole blood, packed cells, blood fractions, or substitutes—was the responsibility of the clinician, who alone could decide this. In therapy, there were the acute or semi-acute emergency procedures, nearly always done on in-patients, to combat severe shock or haemorrhage, and the long-term courses of transfusion, conveniently done in a special out-patient clinic, for the treatment of, for example, aplastic anaemia, leukaemias, and various refractory anaemias. Dr. Wilkinson then described his large out-patient transfusion clinic for the latter type of patient. One such patient had had 179 transfusions of packed cells into the same vein over a period of four years. This year in 269 out-patient transfusions there had been only two febrile reactions.

Blood transfusions, he said, were unnecessary and might even be dangerous when given for blood diseases (for example, pernicious anaemia, hypochromic microcytic anaemias), for which there was perfectly good, potent medical therapy.

Transfusion Reactions

Dr. F. STRATTON, Director of the North-west Regional Blood Transfusion Service, began with the observation that some 50,000 pints of blood were collected by the Service in a year, and since donors were called by name and not by group it might be some time before rare groups became available for a particular patient. The speaker then reviewed the method of collection and storage, pointing out that the leucocytes and platelets did not keep with routine methods, and in any case there was no evidence that the total leucocyte count could be raised by transfusion, while platelets lasted in the body only for a few days even when special methods of collection had been used. Transfusion reactions were due to four factors (assuming the blood was correctly matched): pyrogens, which could be present in chemicals or due to bacterial growth in distilled water; a too rapid speed of transfusion; the administration of small quantities of air; and a sensitivity to plasma, which was found in the recently delivered woman or where there had been abortion. Such reactions could be avoided by giving the blood slowly in a carefully estimated amount, by warming the patient but *never* the blood, and finally by a careful cross-match, which should include a saline agglutination and the Coombs test for incomplete antibody, using a serum which was both potent and specific.

Dr. R. F. JENNISON, speaking as a hospital pathologist who was responsible for the operation of a blood bank, thought that two of his main tasks were the organization of the technical procedures relating to the issuing of blood, and persuading the clinicians to co-operate with him. The giving of blood should be regarded as a major operation. The organization of transfusions was not welcomed by the pathologist, but it had to be done; and certain safeguards had to be introduced to avoid accidents. For instance, the refrigerator in which the blood was kept must be locked, and only specified persons allowed to take blood from it. Much of the ritual of transfusion management might seem irksome, but it had been made necessary by the increasing number of accidents and the accompanying litigation.

Discussion

In the discussion, Dr. R. W. FAIRBROTHER said that it had been carelessness and not the introduction of new groups and techniques that had been responsible for some recent transfusion disasters. There seemed to be a lack of appreciation of this problem by clinicians, who often left the decision about transfusion to the most junior member of his team. Mr. H. A. HAXTON said that in severe shock he favoured intra-arterial transfusions, even aortic transfusion being relatively easy. He thought this would probably appeal greatly to the Blood Transfusion Service, because the condition of the patient improved rapidly with less blood than was given by the intravenous route.

JOHN RADCLIFFE

AN OXFORD BENEFACTOR

A stone tablet in memory of Dr. John Radcliffe was unveiled in the church of St. Mary the Virgin, Oxford, by Lord Cottesloe, on October 17. Radcliffe was buried in the church in 1714. The stone was dedicated by the Bishop of Oxford, Dr. K. E. Kirk. Its erection fulfils a wish expressed by Radcliffe in his will, but forgotten until attention was drawn to it in a recent biography. The ceremony was attended by the Vice-Chancellor (Sir Maurice Bowra), the Radcliffe trustees, members of Convocation, and representatives of the various faculties.

Radcliffe was born about the year 1650. He studied medicine at Oxford, where he graduated M.B. in 1675, becoming M.D. in 1682. Two years later he removed to London and speedily built up a large and lucrative practice. In 1686 he was appointed physician to Princess (later Queen) Anne, and in the following year was elected F.R.C.P. In 1713 he became Member of Parliament for Buckingham and retired from practice. He died in 1714.

The best picture of Radcliffe is perhaps that drawn by William Macmichael in the *Gold-headed Cane*, and Osler once said: "Radcliffe is remembered, first by the Gold-headed Cane, second by never having written a line, and third by the superb monuments which exist to his memory." These include a famous library and observatory, a great infirmary, a college quadrangle, and some travelling fellowships.

Among the directions of Radcliffe's will was a bequest of £40,000 for the building of a library in Oxford, the Radcliffe Library, which was opened in 1749. In 1811 it was decided that the library should be limited to books on medicine and natural science, and in 1861 the Radcliffe trustees placed the building at the disposal of the Bodleian Curators and transferred the scientific books to the museum. Radcliffe also bequeathed his Yorkshire estate to University College, Oxford, to found two travelling fellowships, and he gave £5,000 for the enlargement of the college. His residual estate provided for the erection of the Radcliffe Infirmary and the Radcliffe Observatory.

Nova et Vetera

MICHAEL SERVETUS

"One truth from an enemy is worth more than a hundred lies from our friends."—SERVETUS.[1]

In the outskirts of Geneva, shortly before noon on October 27, 1553, Michael Servetus, physician and theologian, was burnt alive at the stake. Although this dreadful fate was in no way attributable to his revolutionary physiological concepts, and although his contributions to medicine were but a small part of his life's work, it is fitting that we should remember him on this the quatercentenary of his death.

Servetus was born in 1511 at Villanueva (Aragon) in Spain, and at an early age demonstrated unusual intelligence and a delight in the attainment of knowledge. His first work, *De Trinitatis Erroribus* (1531),[2] published when he was only 20 years of age, was a heretical revolt against accepted theological doctrines and won him the universal condemnation of the Church. Taking up the study of medicine in Paris, where he was a contemporary of Andreas Vesalius, he displayed the same diligence of labour and originality of thought that had characterized his pursuits in other fields of knowledge. A year after graduation he published a book on syrups,[3] a subject that to us seems innocuous enough but which in those days evoked the opposing principles of Galenic and Arabian medicine. This work contains a statement that epitomizes his life's endeavour: "That I may not withhold from others that which I possess myself and gratefully acknowledge, which may be of use to my fellow-men, I throw aside fear and proclaim what I believe to be the truth."[4] Among other subjects, he studied and taught judicial astrology and thus was accused of divination.

Leaving Paris, Servetus settled in Vienne, Dauphiny, where he quietly practised his profession under the patronage of the archbishop. Here he remained until 1553, when at the age of 42 years he came into violent and fatal conflict with, first, the Papal authorities and then John Calvin, because of the outspoken heresies contained in his book *Christianismi Restitutio*.[5] Also in this book is an account of the pulmonary circulation, repudiating the authority of Galen, which still dominated medicine, and at a time when deviation from it was nowhere evident. It was not, however, noticed to be of physiological importance until 1694,[6] 78 years after Harvey's initial enunciation of his theories on the circulation of the blood. To-day, it seems likely that Servetus was not in fact the first to describe the lesser circulation, for an Arabian physician, ibn-al-Nafis, mentioned it in 1268.[7 8] His own conclusions, however, are not made the less important by this more recent knowledge; the 300 years that separated these two independent thinkers had seen no radical change in medicine.

There has been considerable argument on Michael Servetus's place in history, and this is embodied in the extensive literature accumulated over the four centuries since his death. Be this as it may, his legacy to medicine, although taking no part in the shaping of man's concepts of the blood's circulation, is nevertheless a landmark at the dawn of physiology. Here was a man of independent thought and in advance of his time, who had the steadfastness of purpose to pursue his unorthodox theories, although cognizant of the fate awaiting dissenters from the accepted beliefs. It is typical of the man than even when the flames were devouring him he would not recant. Such men should not be readily forgotten.

EDWIN CLARKE.

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MONUMENT TO SERVETUS

Champel, the scene of Servetus's execution, lies in the outskirts of Geneva. At the junction of the Avenue de la Roseraie and the Avenue de Beau-Séjour, facing the

imposing cantonal hospital, stands a monument in memory of Servetus, erected in 1903. Close by is the little Chemin de Michel Servet. The monument, which is illustrated above, bears the following inscriptions (translated).

On the front:

> 27 October, 1553, there died at the stake at Champel, Michael Servetus, of Villanueva, Aragon, born 29 September, 1511.

On the reverse:

> We the respectful and grateful sons of Calvin, our great reformer, though condemning an error which was that of his century, and firmly attached to liberty of conscience according to the true principles of the Reformation and of the Gospel, have raised this expiatory monument, 27 October, 1903.

A translation of the description of the lesser circulation is also in *Michael Servetus a Translation of His Geographical, Medical and Astrological Writings*, by C. D. O'Malley, London, Lloyd-Luke, 1953, p. 204. This book also reproduces the title-page of the copy of *Christianismi Restitutio* in the Bibliothèque Nationale, Paris.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Clinical Pathology in General Practice

Sir,—As a hospital pathologist I am following with interest your series on clinical pathology in general practice.

Professor S. P. Bedson's view (*Journal*, October 3, p. 774) that the service should be a consultant one and not "just the provision of laboratory aids for general practitioners" is admirable. It suggests to me that the consultant should be a clinical pathologist in the widest sense, able to discuss with the practitioner the advisability for certain investigations, carry them out in his laboratory, and finally place all the results in their correct perspective.

Both Professor Bedson and Dr. M. T. Parker, of the Public Health Laboratory Service (*Journal*, October 10, p. 823), rightly deprecate slot-machine pathology, yet the latter makes the astounding statement that "it is best to make inquiries locally if there is any doubt about the correct laboratory for any particular specimen." He apparently divides clinical bacteriology into infectious and non-infectious, generously allowing the hospital pathologist to culture the urine. He will examine the blood for glandular fever, but he does not mention leukaemia. Is this also given to the hospital pathologist? He makes a general examination of the cerebrospinal fluid. I assume this includes the quantitative chemical analysis; or is the supernatant fluid transported to the hospital laboratory? Perhaps the patient undergoes two lumbar punctures.

After studying both your articles the reader can only assume that the hospital pathologist and the public health bacteriologist meet on the patient's doorstep, there to agree more or less amicably on the division of the spoils. It would be equally sensible to arrange for the attendance of a haematologist and a biochemist. Dr. Parker has given us an admirable review of the facilities available to the general practitioner, but I question seriously whether the public health laboratory should undertake clinical bacteriology unless it is prepared also to carry out full biochemical, haematological, and even histological investigations as well. It is perhaps unnecessary to point out that it would then no longer be a public health laboratory.

A sensible solution to the problem, at least in my own experience, is to have the two organizations under one roof. Only then can that happy co-operation be achieved by which the practitioner is able to get a comprehensive opinion on his problem.—I am, etc.,

Sheffield. A. J. N. Warrack.

Orthopaedic Care in Poliomyelitis

Sir,—Sir Reginald Watson-Jones and Mr. H. J. Seddon in their letters (*Journal*, October 10, p. 828, and October 17, p. 884) regret that orthopaedic surgeons are not being adequately consulted regarding the treatment of the acute stage of poliomyelitis. All will agree that orthopaedic surgeons must play a very large part in the battle against the disease and its effects, but it may be pointed out that the interest of most orthopaedic surgeons is centred around the prevention of deformity, and not on those factors which endanger life. So much is this so that the treatment advised by them may conflict very seriously with what is needed to prevent lung complications. Further, the prevention of contracture and deformity in the first few weeks is surely a simple matter which can be dealt with by properly trained nurses.

If orthopaedic surgeons are prepared to become expert in all aspects of the acute stage of the disease, then they will indeed be welcome when difficulties arise, but they will have to learn about the "whirring pumps and whistling tracheotomy tubes" which Mr. Seddon belittles. On the whole they may well prefer to concentrate their efforts on the later stages when the need for their special skill is most apparent.—I am, etc.,

Oxford. W. Ritchie Russell.

The Human Foot

Sir,—I have read with interest the articles (*Journal*, October 3, pp. 745 and 749) and annotation (p. 772) on the subject of foot deformity, and write to make the following observations.

The normal position of the hallux is quite straight, and therefore any departure from this position *in the foot at rest* is deformity. Until quite recently slight deviations from the normal position of the hallux were dismissed as unimportant, but I have shown[1] that such slight deviations are of vital importance and are the first signs of hallux valgus. Failure of many observers to appreciate the importance of, and to record, these slight deviations may well account for the wide variation in reported incidence.

Correctly designed footwear must accommodate the hallux quite straight, and any deviation from this will set in motion the changes leading to proximal hallux valgus. Whatever predisposing factors there may be, almost invariably a pressure on the inner side of the phalanx greater than that on the inner side of the metatarsal is necessary to start the changes leading to deformity.

Such pressure is given by footwear without a straight inner border. The most urgent requirement to reduce the appalling incidence of acquired foot deformity is an adequate supply of correctly designed footwear, especially in the cheaper lines.

It is not surprising to me to learn that Dr. Doris A. Craigmile (p. 749) found the highest incidence of badly fitting shoes amongst the older girls. Neither the girls nor their parents are to blame. A tour of the Shoe and Leather Fair (Olympia, October 5 to 9) failed to discover a single pair of shoes for the late teenager or for an adult that would accommodate the hallux in its normal position. I find therefore that I cannot agree with Dr. Craigmile when she states: "No single cause for the predominance of hallux valgus in girls is apparent." With each teenage year their footwear grows more pointed. The very firms that acquired their custom by "straight inner border" publicity supply to the teenage girl, but still under the same trademark, footwear that deforms. The girls and their parents have no choice; they cannot buy correctly designed footwear.—I am, etc.,

London, S.E.22. Charles A. Pratt.

Reference

[1] *Your Children's Feet*, 1951. London

Sir,—From the rising volume of articles on feet which have appeared recently in the medical press, including those in the *Journal* of October 3 (pp. 745 and 749), it may be hoped that, after having been regarded for many years as of minor importance, feet are at last beginning to have the attention they merit. From research workers, from medical officers, and from chiropodists come columns of figures which, correctly interpreted, should add enormously to our knowledge of the foot problem and especially of the incidence of disorders. It is most gratifying to see during recent years the improvement in available footwear, particularly for children, and to hear of the research undertaken by the shoe trade into foot problems. But, apart from focusing attention on an evil, are all these pages of figures going to tell us much more than two things we already know—namely, that the incidence of foot troubles is shockingly high, and that very many of them have their origins in childhood and youth?

I would wish to put forward two aspects that appear to be generally overlooked in the search for foot health. The first is that foot health is to a very large extent dependent on the straightness of the toes. The integrity of toe func-

tion depends chiefly upon the development, exercise, and a continual ability to use the smaller intrinsic muscles of the foot whose most important work is to provide a mechanism which prevents the toes from elevating and bending into the clawed or retracted position. In childhood, bedclothes, bootees, socks, and shoes militate against the development and function of these muscles, and in adult life the wearisome daily exercises often prescribed are poor compensation for lessons which the musculonervous system should have learned in childhood. The forefoot is essentially a mobile structure which gains and keeps its health by walking unencumbered on uneven surfaces; the interposition of a sole, no matter how free the toes, tends to reduce the sensory stimuli which are needed for the development of the intrinsic muscles.

The second fundamental difficulty concerns the "anomalies" of the foot. There is a growing tendency to catalogue and incriminate all minor variations in the structure of the foot from the height of the arch to the angles between the metatarsals. Indeed, some would have us believe that man's foot disabilities are largely due to such conditions as "short" first metatarsals or any other bone which does not come up to an imaginary standard. It is an interesting thought that man, despite the effects of selection, is unlikely to be alone among the mammals in not always being born perfect, but compared with other animals he has the grave disadvantage that he is often unable to compensate for these anomalies either because his toes, whose function has not been developed in youth, are not in control of the situation, or because his method of compensation becomes in fact pathological, since he is compelled to wear shoes. Among those who have never worn shoes an adjustment to compensate for peculiarities in structure occurs naturally and without discomfort, but in the shod foot in which the muscular mechanism is in any case below the standard of the bare foot such compensations tend to produce well-recognized pathological conditions. One can instance strong use of the big toe in the very mobile unshod foot as a factor in securing stability, but the same action within a shoe tends to become a pathological flexion of the hallux.

My belief is that with few exceptions babies are born with sound feet and that in spite of anomalies they can grow into healthy adult feet if given the chance. If shoes are blameworthy it is necessary to find out the reason in the fullest sense and not merely to confine the investigation to the contour of the shoe. It does appear that the time has arrived when surveys of incidence have served their purpose and that the fundamental causes of foot disturbances during growth should now be considered.—I am, etc.,

London, W.1. JOHN HANBY,
President, Society of Chiropodists.

Alcohol-induced Pain in Hodgkin's Disease

SIR,—I read with great interest the article entitled "Alcohol-induced Pain in Hodgkin's Disease" by Dr. Jan G. de Winter (*Journal*, September 12, p. 604).

It will interest you to know that one of my assistants, Dr. R. Verbeke, published a similar case, observed in my department, in *Belgisch Tijdschrift voor Geneeskunde*.[1]—I am, etc.,

Ghent, Belgium. L. REMOUCHAMPS.

REFERENCE

[1] *Belg. T. Geneesk.*, 1952, **8**, 993.

SIR,—I was most interested in Dr. Jan G. de Winter's article "Alcohol-induced Pain in Hodgkin's Disease" (*Journal*, September 12, p. 604). In view of the scanty data available on the subject I thought the following case might be of interest.

A male aged 28 years was referred to hospital in December, 1950. His first complaint was that 18 months previously he had noticed severe pain in the region of his left shoulder on taking alcohol. It was not until 10 months later that he first noticed enlarged glands in the left side of the neck. On examination, the patient was in excellent general condition. There were multiple enlarged glands in the left side of his neck, two enlarged nodes in the left axilla, but no other enlarged glands were felt. Section of glands from the left neck showed Hodgkin's disease. Throughout the course of the disease the patient had been an in-patient on many occasions, and it was noted that he always refused alcoholic drinks because he felt alcohol disagreed with him.—I am, etc.,

London, W.C.1. D. CROWLEY.

SIR,—Dr. Jan G. de Winter states (*Journal*, September 12, p. 604) that no case report describing this symptom seems to have been published in this country so far. He is wrong. The abstracters and indexers take no note of letters to the editor, though sometimes such letters contain important information. For example, the first report of jaundice following serum given to prevent measles was published in a letter to the editor.[1]

I recorded the first case of alcohol-induced pain in Hodgkin's disease in this country in the *Lancet* in 1952.[2] To make such a first description is always gratifying, as one feels that one has been unusually observant even if aided by an inordinate share of luck. One may even have a vague hope that one day one's name will be attached to the disease or syndrome. However, as I happen to be the patient also, I will continue to call myself,

ANON.

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[2] *Lancet*, 1952, **2**, 640.

Cancer and the Public

SIR,—Just before Christmas, 1952, a man aged 46 went to his doctor complaining of a lump in his throat. At other times he complained of difficulty in swallowing, and he continued to complain. About July, 1953, a gland appeared in his neck, and soon after that he was admitted to hospital and a tracheotomy was found to be necessary. Examination of his pharynx revealed an extensive cancerous growth of the deep pharynx on the left side. Deep *x* ray was not considered advisable, and exploration of the tissues of his neck showed the growth to be inoperable.

With all the power of television and radio behind us surely it is possible to organize better education, not only of the public, but also of ourselves.—I am, etc.,

Liverpool, 7 JOHN MCFARLAND.

Phenylbutazone

SIR,—I agree with Dr. Bowman Edgar (*Journal*, August 29, p. 511) that the dosage of phenylbutazone should be as small as possible. Many cases can be controlled with 200 mg. per day, and more than 400 mg. per day is rarely necessary. If this dose gives no relief within five days, treatment should be discontinued, and the same dose tried again in three weeks. Out of a total of 415 patients, 54 failed to respond at a first trial of the drug; but 37 of these responded at a second or a third trial.

As soon as the pain has been relieved with 400 mg. daily, the dose should be reduced to 300 or 200 mg. In 57 patients who were able, after the first 7 to 10 days, to carry on with 200 mg. daily, complications have been less than half as common as in 210 earlier patients who had continued for several weeks on 400 mg. or more daily. Moreover, the complications when they do occur on these reduced doses are milder. Treatment should be interrupted as soon as complications appear and resumed when they have passed off; 106 out of 355 patients had complications which caused interruption of treatment, and in 86 of these treatment has proceeded in spite of one or two interruptions.

The 20 patients who could not proceed were: 3 with congestive heart failure (all in patients over 70); 4 with

haemolytic or microcytic anaemia in patients who had previously had anaemia; 11 with recurrent gastritis with or without ulceration (6 had had stomach trouble before and 6 were over 65 years); 1 with severe melaena (aged 69); 1 with recurrent oedema of feet (aged 79). There have been no cases of neutropenia. Complications have been more frequent and more severe in patients over 65 years of age. 102 of the 106 complications appeared in the first five weeks. A study of the voluminous literature indicates that most of the toxic effects have appeared as early as this. I believe that the patients are safe when they have been guided through this critical period.

To me phenylbutazone is the most valuable drug which has yet appeared for the treatment of rheumatic disease. In its action on acute synovial inflammation it resembles cortisone, but it is much superior to cortisone in the wide range of rheumatic disorders which it relieves so decisively that it must be called a specific antirheumatic drug. It is not a general analgesic, because it has failed to relieve 30 patients with a dozen non-rheumatic disorders.

Like most other valuable drugs, phenylbutazone in its early history has been used in doses larger than necessary. I believe that most of its serious effects have come either from overdosage or from giving it to patients who are either too old or otherwise unsuitable (over 65 years or suffering from diseases of blood, cardiovascular system, or alimentary tract).—I am, etc.,

London, W.1. MICHAEL KELLY.

A.C.T.H. and Cortisone in the Schönlein–Henoch Syndrome

SIR,—In the article by Drs. D. G. Adamson, W. Walker, and A. E. Macintosh (*Journal*, September 19, p. 656) it is claimed that A.C.T.H. and cortisone are of value in the treatment of the Schönlein–Henoch syndrome. This claim is based on their one case and several other early case reports.

This disease is characterized by its spontaneous remissions and exacerbations, and no such claim can be made for any drug unless its effect is consistently good in a number of cases. In Sheffield we have studied and reported[1] nine children with this disease treated with A.C.T.H. and/or cortisone, and were forced to the conclusion that these drugs are virtually useless. The severe constitutional disturbance which sometimes accompanies the disease may be alleviated by the drugs, however, and it would seem justifiable to give them only to patients so affected.—I am, etc.,

Sheffield. M. G. PHILPOTT.

REFERENCE

[1] Philpott, M. G., and Briggs, J. N. (1953). *Arch. Dis. Childh.*, **28**, 57.

Encouraging Drug-resistant Tuberculosis

SIR,—In these days of an enlightened popular press our professional colleagues may be pardoned for yielding, against their better judgment, to the demands of patients and their relatives for treatment of some sort or other where no known form of therapy is of any avail. This is particularly true in the case of the sufferer from advanced tuberculosis, who may insist on having the "wonder" drugs that have of late been so frequently brought to the notice of the general public. That such persons can quickly harbour drug-resistant tubercle bacilli would not appear to be of very much consequence. The drowning man must have his straw.

A young man of 25 with tuberculosis, who had been under my observation for the last nine years, steadily went downhill until eventually enormous cavities developed in his lungs, and he died. I was told by his mother that during the last 18 months of his illness he had walked to his doctor's surgery once a week to receive an injection of streptomycin, largely at her request. How many streptomycin-resistant organisms he must have coughed up I cannot imagine, but it is a worrying reflection that this type of case is by no means uncommon, and that if the therapeutic folly of giving such "treatment" to advanced chronics continues we shall in due course find that our antibiotic drugs are useless.—I am, etc.,

Wolverhampton. ARCHIBALD OGG.

Peripheral Neuritis Following Tetraethylthiuram Disulphide Treatment

SIR,—I was interested in the report by Dr. F. B. Charatan on a case of peripheral neuritis following tetraethylthiuram disulphide treatment (*Journal*, August 15, p. 380), and would like to report a case of apparently the same condition which came under my care three weeks ago.

The patient was a man of 28. He was not an alcoholic, but used to go on frequent "binges," which, becoming more frequent, worried him. He went to a doctor 12 months ago and was advised to take tetraethylthiuram disulphide ("antabuse"), one tablet daily. This he did for about two weeks and then very irregularly for a further two months. After that his binges recurred, though not so frequently. Four weeks before coming to me he had restarted the tetraethylthiuram disulphide and had taken one tablet every day diligently. He had had no alcohol during that four weeks, but during the last week of it he noticed extreme tiredness, and he was inclined to fall asleep during the day at his work (he is a clerk) in spite of a good night's sleep. This was the only presenting symptom.

As a result of a hurried examination I decided to try him on dextroamphetamine sulphate, one tablet morning and noon, and told him to report to me in three days. Three days later he came back very satisfied with the dextroamphetamine sulphate tablets, which he said worked "like a charm," and then he told me that he had forgotten to mention at the first examination that as well as tiredness he had tinglings, to the extent of being even painful, in the palms of his hands and soles of his feet since about the same time as the tiredness assailed him, and he had discovered that his calves were tender. I examined him again. His knee jerks were brisk, but the calves of his legs were indeed extremely tender. He then told me about the tetraethylthiuram disulphide for the first time. At this stage I was unaware of this effect of tetraethylthiuram disulphide, and treated him with 100 mg. vitamin B_1 daily intramuscularly for five injections. A week later he was symptom-free.

I examined him again after reading Dr. Charatan's report, and he told me he had stopped the tetraethylthiuram disulphide since the first interview three weeks ago and that he was now feeling perfectly well in every way.—I am, etc.,

Ndola, N. Rhodesia. W. K. BARRY.

Infective Hepatitis in Doctors

SIR,—In your annotation on "Infective Hepatitis in Doctors" (*Journal*, September 12, p. 614) you quote Madsen[1] as being surprised that the incidence of infective hepatitis seems lower in hospital nurses than in doctors, presumably G.P.s. Possibly the conclusions we came to as regards the mode of spread of infective hepatitis in a West African brigade in Burma in 1944 may be of interest. For reasons we will give later it seemed that the disease spread rapidly whenever overcrowding took place. Also the infectivity was at its greatest in the pre-icteric stage, and the incubation period seemed to be about 21 days. Those are the conclusions we R.M.O.s came to, but we think the whole story is worth telling.

Infective hepatitis was becoming a serious problem in our West African brigade, then in Burma. In addition it was suspected that occasionally an African soldier would go sick with yellow eyes almost indistinguishable from those seen in jaundice but caused by instilling a mepacrine tablet dissolved in saliva into the conjunctival sac. Hence the battalion M.O.s were on the alert, and all cases with symptoms suggestive of the onset of infective hepatitis were examined for bile in the urine, and a careful close-up look at the conjunctiva was done. About three weeks from the start of these close-up examinations two of the three battalion medical officers went sick with infective hepatitis. To our surprise we found that there was very little infective hepatitis in the third battalion, which was in the same area. Eventually we

concluded that the reason for the low incidence was that the Africans in that battalion did not sleep in pairs as they did in our two units so as to double the number of blankets in the cold weather. It was this pairing which gave us presumptive evidence of the incubation period, and time and time again two sleeping companions would go sick with infective hepatitis at intervals of about 21 days. This of course suggested an incubation period of approximately 21 days, and that the disease was transmitted during the pre-icteric stage. We also noticed that, even though base hospitals had numerous patients suffering from infective hepatitis, fresh cases seldom occurred among nurses and hospital staff. This we thought due to the fact that the cases were not usually admitted in the pre-icteric stage.

We feel that, even if our observations are similar to other observers', at least they give an answer to Madsen's query. Also they reinforce the "close contact respiratory spread" theory, and suggest that, for that particular outbreak, infected food and infected syringes can be exonerated. In lighter vein, do our observations not suggest that patients with symptoms suggestive of early infective hepatitis should be made to turn their heads slightly away from the examiner when being examined for conjunctival icterus?—We are, etc.,

W. J. C. HILL.
J. WEIR.

Portrush.

REFERENCE

[1] *Ugeskr. Læg.*, 1952, **114**, 951.

Post-gastrectomy Syndrome

SIR,—The profession is much indebted to Mr. J. Ewart Schofield and Mr. P. St. G. Anderson for their studious and comprehensive review of the surgery of peptic ulcer (*Journal*, September 12, p. 598). We appreciate their indomitable spirit shown by a fresh effort to eliminate the bane of partial gastrectomy—the tithe of patients who, instead of gaining the happy relief of the majority, develop a miserable and intractable malady.

When giving the results of my experience in this sphere, gained before I ceased general surgery, I was moved to allude to a possible alternative remedy.[1] Operation was unsatisfactory in two respects—it entails ablation of three-quarters of a large, important, apparently healthy organ on account of an ulcer usually about 2 cm. in diameter, and it incurs a 10% risk of establishing a miserable disability. Might not either drawback give us furiously to think?

With commendable tenacity surgeons have tried extensively during the half-century to devise an operation offering uniform success. Are we faced with a "brick wall" so far as the refractory 10% are concerned? The disease is not a simple mechanical lesion like hernia, but of complex aetiology. Is it unreasonable to question the amenability of the obdurate fraction and to try a new approach to the problem for this miserable minority? Meanwhile, undoubtedly, surgeons may well agree to the proposed retrial of one of the earlier surgical remedies. May I humbly suggest a campaign of clinical research to unravel the distinctive qualities that may demarcate the refractory type?—I am, etc.,

A. WILFRID ADAMS.

Bristol, 8.

REFERENCE

[1] *Med. Press*, 1949, **221**, 335.

Splenic Venography

SIR,—I read with interest the paper by Drs. N. R. Konar and A. N. Sen Gupta (*Journal*, October 10, p. 810). In the course of the last 20 months we have carried out splenic venography on 50 occasions with results about to be published.

Drs. Konar and Sen Gupta describe two normal splenograms. With large experience they would have found that dilatation and tortuosity of the splenic veins are observed under normal conditions and are therefore of no clinical significance. Quite frequently during the process of puncture the spleen is pushed an inch or two medially, with resulting tortuosity of the veins. Figs. 1 and 2 in their paper show spread of the dye into the splenic capsule, indicating insufficient penetration of the needle. This explains the authors' statement that most of the patients complained of pain. Splenic venography in our experience is entirely painless, provided the needle is well within splenic tissue.

The authors state that the radiological appearance may be a measure of the degree of hypertension. We cannot confirm this. An apparently normal splenogram was observed by us in cases of proved portal hypertension. One of our cases with cirrhosis of the liver (proved at laparotomy and necropsy) had splenic venography carried out monthly from March, 1952, until May of this year. At times in this case we could demonstrate anastomosis with the left coronary vein and with oesophageal branches of the left gastric vein, and at other times a normal flow into the portal vein and its intrahepatic branches was observed.

Much more knowledge, particularly of the appearances under normal conditions, is needed before the diagnostic value of the method can be assessed.—I am, etc.,

H. FULD.

Liverpool

Tuberculosis Classification

SIR,—A complete and satisfactory classification of tuberculosis involves complete knowledge of the pathogenesis of the disease in all its forms. Such knowledge does not, of course, yet exist. Attempts to reach it must employ many diverse methods, one of which is intelligent and imaginative observation of an immense amount of material over a long period. Who would deny that the basis of most discoveries is a flash of insight following intensive study of a subject, and succeeded by prolonged painstaking practical work upon it?

My book, *The Classification of Pulmonary Tuberculosis*, reviewed in the *Journal* of September 26 (p. 715) by Dr. J. G. Scadding, is a result, on the one hand, of failure to obtain satisfaction from all existing classifications, and, on the other hand, of the satisfaction which I experienced when I brought in the "type of disease" as a factor additional to the official British and American classifications. By doing this I found that the natural history of each form of the disease was covered. I have applied my classification in practice to over 6,000 cases. It is true that in the book I have fully described and classified only 62 cases, but these are only samples and the classification has actually been applied to the whole of my material accumulated over some 30 years. Dr. Scadding would seem to mislead your readers when he ignores this practical basis of my classification and dismisses summarily my ideas as "unproved" and "based on theoretical considerations."

Again, Dr. Scadding seems to uphold what he calls the "modest virtues" of a classification "based on no more than the extent of the disease and the presence or absence of bacilli" (i.e., Turban). The official British and American classifications go further than this and include a third factor, "degree of activity." My classification goes still further and includes, in addition, "type of disease," which is the most important of all for the reasons stated above. Take this case, for example: "A.B. has pulmonary tuberculosis involving as much as a part of one zone and with sputum positive." This classification is based purely on extent of disease and presence or absence of bacilli, and would, according to Dr. Scadding, have the modest virtues of "creating no confusion and implying no unproved hypothesis." Would it? As I see it, this classification could be applied to any one of four quite different forms: benign primary, malignant primary (i.e., two primary forms), a minimal lesion, or localized chronic miliary tuberculosis (i.e., in my classification two post-primary forms). All four of these forms could be of the same extent and with sputum positive. But what a difference in their pathology, natural history, course, prognosis, and management. Is this not confusion, and unutterable confusion at that, which every tuberculosis worker has moreover experienced? Does Dr. Scadding really recommend that the clock should be put back 50 years?

Dr. Scadding, using the great prestige of his name and position, has seen fit to review my work in a purely negative

manner. I hope, on reflection, that he will consider this unfair both to your readers and to my obscure self. A true and acceptable judgment can surely only be formed by actual trial.—I am, etc.,

London, N.W.8. MILOSH SEKULICH.

The Broken Acrylic Head

SIR,—The Judet arthroplasty is only a step in the development of arthroplasty of the hip. The design of the prosthesis is not perfect and will be modified before the best possible design has been arrived at. The present design is only satisfactory and gives good results provided that the head is so placed that the weight is evenly distributed on the rim and on the stem, and that the head is placed in healthy bone with a reasonable blood supply. The result will be satisfactory provided the fitted prosthesis does not rotate, become loose, or tilt, transferring all the weight to the rim, which sooner or later will break (Fig. 1). After the rim has broken the whole weight comes on to the stem, which is not strong enough to stand the strain, and therefore a fracture occurs.

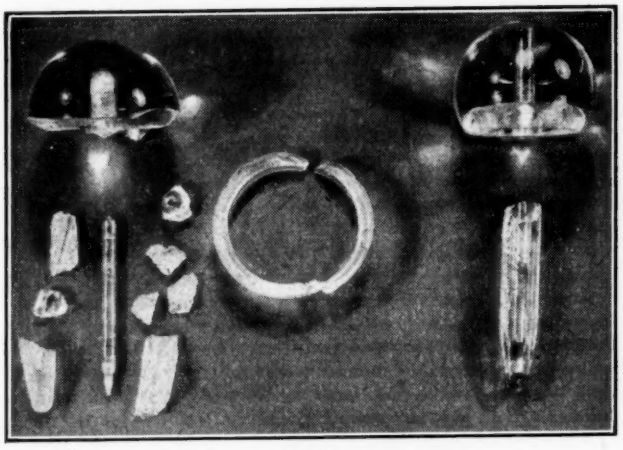


FIG. 1

In my experience, 6% will fracture in the first two years after the operation, and, after a longer interval, the breakage rate will probably be very much greater. I know of three cases of fractures in my own series, and of three cases belonging to other surgeons. An examination of these broken heads suggests that the rim fractures first, and that the stem will not support the weight of the body without the rim taking a large proportion of that weight. The metal insert is too small to be of any use and only weakens the acrylic stem, which would, in my opinion, be much stronger without the present metal insert. Shearing tests have proved this to be a fact.

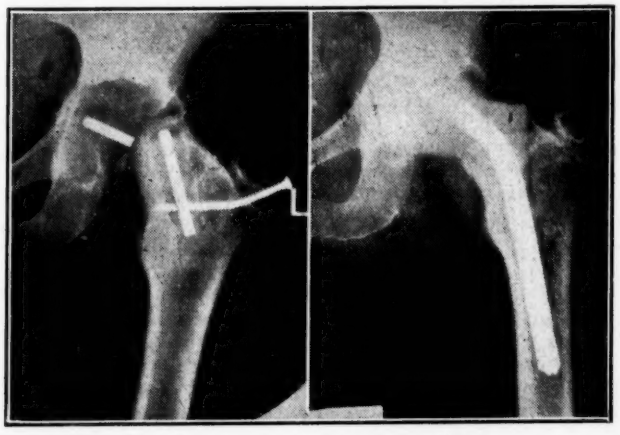


FIG. 2 FIG. 3

The signs and symptoms of a loose prosthesis are pain and spasm of the hip with marked deterioration of function once a fracture of the acrylic head has occurred. After two years of vigorous use, appreciable wear of the rounded head can be seen. Following a fracture of the rim and neck (Fig. 2), the case presents as a typical fracture of the neck of the femur, with external rotation, shortening, pain, and spasm.

The treatment of these cases of broken acrylic heads is a problem which must be faced. The fitting of a larger prosthesis of the same design does not solve the problem. A much more extensive prosthesis, such as that shown in Fig. 3, is a very satisfactory method of overcoming this problem, and gives excellent results.

I feel that the present Judet head is going to cause considerable trouble, and should be supplanted by a prosthesis which is more adequately anchored in a situation where the circulation of the bone is not affected by the disease process.—I am, etc.,

Bristol, 8. K. H. PRIDIE.

The General Practitioner and the Psychiatrist

SIR,—I should like to make two comments on the interesting article on this subject by Dr. N. J. Bodkin and others (*Journal*, September 26, p. 723). The authors state (p. 724): "Unlike the depressive illnesses, it is not essential to treat neurosis." To many of us this will seem not only a sweeping but a hazardous generalization. The patient who "suffers agonies" (his own words—but there is no reason to disbelieve him) when he has to travel to work in a crowded bus or train; whose sleep is greatly disturbed; who grows increasingly agitated and distressed; who may become housebound and in the end bedridden—this patient is suffering from a neurosis. But is it therefore "not essential" to treat him?

I wonder if it is true that the "majority (of marital problems) can be dealt with satisfactorily by the general practitioner." Many doctors and many patients would dissent. A great deal depends on the personality, experience, and emotional maturity of the practitioner; but there are other considerations. Most of such problems are caused, or at any rate complicated, by the projection upon the marriage partner of unresolved and indeed unconscious conflicts, which to be properly understood and wisely handled require psychological skill, knowledge, and training. Not every G.P. is so equipped to deal with them. If "a legal and not a psychiatric opinion is indicated," this is often because "the psychiatric symptoms [which] have arisen as a result of marital disharmony" have been disregarded too long. It would be unfortunate if your readers were left with the impression that patients with marital troubles should be referred to a psychiatrist, not because he is likely to be of much help, but because he will relieve the G.P. of the nuisance of "legal entanglements."

Stresses and strains within the marriage relationship, severe enough to be brought to the doctor's notice, may often, if properly treated, lead, not to the solicitor's office and thence the divorce court, but to a greater self-knowledge on the part of husband and wife, and in the end to a more stable and fruitful relationship.—I am, etc.,

London, W.1 G. L. RUSSELL.

Modified Leucotomy Operations

SIR,—Dr. William Sargant's contribution (*Journal*, October 10, p. 800) is of immense importance in that it widens the applicability of leucotomies to almost universal proportions. He states: "Psychiatry often creates insoluble difficulties for itself when we leave the patient's bedside and become too involved in speculative philosophical issues." But leucotomy is the only operation performed for ill-defined reasons on healthy tissue by a technique which is purely and irrevocably destructive, and for a therapeutic result which is often unpredictable. Dr. Sargant maintains, not surprisingly, that these patients with the best-preserved personalities will

do best. If ethical considerations are to be so largely discounted, what criteria must we use for *not* performing a leucotomy? Most general practitioners will agree that a good quarter of their patients would obtain symptomatic relief with a limited frontal cut.

"The criterion of success or failure," Dr. Sargant continues, "is best measured by whether the patient and relatives are pleased or displeased." The pleasure of a post-leucotomized patient and his reactions to his operation will obviously be altered by the very nature of his treatment. If the pleasure of patients and relatives is to become the primary aim of therapeutics, then we are reduced to treatment by analgesics and placebos. Even if one crudely regards the brain as a barometer which reflects social and sexual tensions, can we indiscriminately apply a principle of "cure" which merely blunts the sensitivity of the instrument? Psychiatrists, who to-day are playing an increasingly important role in contemporary society, must hesitate before employing a method of therapy which involves the mechanical and qualitative destruction of cerebral tissue—otherwise we shall shortly be having "leucotomy for the millions."—I am, etc.,

Glasgow. LEONARD DAVIDSON.

An American Cottage Hospital

SIR,—Being on a visit of a few months to Washington, D.C., it was my good fortune to be invited to pay a visit to the Calvert County Hospital at Prince Frederick. This hospital so impressed me that a short description may be of interest to your readers.

The hospital, which was opened about the middle of May this year, cost $750,000, or £250,000, to build, and its maintenance works out at $11,000 (£3,660) per month. Patients pay a weekly charge of $9–$20. If they cannot afford this, however, they may get a certificate from their general practitioner which entitles them to treatment free or at a reduced rate. The hospital is a brick-built, one-storied building about a mile from Prince Frederick, a small township some 50 miles south-east of Washington. The wards, which are all two-bedded, face south and the main entrance west. The hospital accommodates 30 patients, but provision is made for extension in the future if needed. The number of occupied beds up to date is 90%. The area served is roughly 400 sq. kilometres, with a population of 12,000.

The beds are divided between white population and coloured, in the proportion of roughly two-thirds white and one-third coloured. Provision is made for surgical, medical, and obstetrical cases, though there are no beds specially set aside for obstetrical cases. There are two labour rooms, one for white patients and one for coloured, and two delivery rooms, also for white and coloured patients, and two babies' rooms to which no one except the authorized nursing staff is admitted. There were four or five babies, white and coloured, whom I saw through the inspection window in their transparent cribs.

Operations are done by the local medical staff and, if necessary, by specialists from neighbouring big towns. Anaesthetics are also given by local doctors and specialists. The two operation theatres are modern and well lighted with "shadowless" lighting, and are air-conditioned. There is also a well-equipped recovery room. *X*-ray equipment is most up to date, with patients' disrobing and dressing room. The radiologist is in a special compartment with a lead glass inspection window so that he has full protection from *x* rays. There is one well-equipped laboratory with technician and consultant if needed. Oxygen is piped to all beds as well as being available in the theatres.

The staff consists of five visiting doctors. Outside doctors are not permitted to treat their own cases, but their visits are welcome. Nursing staff is six registered nurses and eleven unqualified assistants. The administrative staff consists of the superintendent and her assistant, a secretary, and a filing clerk. There is a domestic staff of six, all coloured. Food is under the care of a dietitian, with the help of a housekeeper. Amenities consist of nurses' dining and rest rooms, medical staff rest room, private consulting room, and conference room. Provision is made for visitors any afternoon between certain hours, and there is a room where they can talk privately and have meals with their friends.—I am, etc.,

Petworth, Sussex. D. C. DRUITT.

POINTS FROM LETTERS

Anaesthetic Deaths

Dr. F. J. RUSSELL STONEHAM (Windsor) writes: Deaths occurring under anaesthesia through a tap of the machine being accidentally turned on prompt me to make the following suggestion to the manufacturers of anaesthetic equipment. Could not the cyclopropane cylinder and yoke be mounted between the carbon dioxide and oxygen cylinders on the standard Boyle machine? The key for the cyclopropane would then be right out of harm's way instead of placed as it is now on a vulnerable corner of the machine where it can easily be turned on, especially as the actual valves of the cylinders vary considerably in tightness.

Morphine and Alcohol

Dr. H. RHYS DAVIES (Watford) writes: Your annotation (*Journal*, August 22, p. 437) on the apparent synergistic effect of morphine and alcohol taken together may be of wider application. As long ago as 1935 an annotation (*Journal*, 1935, **2**, 1108) appeared commenting on the work of Danielopolu and his colleagues (*Bull. Acad. Méd. Paris*, 1935, **114**, 342), who had studied the acute intoxication of dogs with benzene and amidopyrine. They showed that the acute toxic effects of these substances may be masked by the barbiturates, but not the chronic toxic effects. The combination of these drugs with the barbiturates therefore possesses certain peculiar dangers in that the immediate effects of overdosage may not be manifest. This observation may not, perhaps, apply to human beings nor to phenylbutazone (which is chemically related to amidopyrine). It would, however, appear to be a wise precaution to avoid prescribing the barbiturates with phenylbutazone.

Pain of Transurethral Manipulations

Dr. W. MULHALL CORBET (Amsterdam) writes: It is refreshing to read such an eminent urologist as Mr. H. P. Winsbury-White (*Journal*, September 19, p. 674) advocating the late Mr. Canny Ryall's use of cocaine for urethral anaesthesia. Mr. Winsbury-White omits two important points—namely, the exact technique of anaesthetization, especially of "milking" the solution back into the posterior urethra; and the fact that a slight wincing or change of countenance on the patient's part is an invaluable indication that the bladder is sufficiently distended with fluid, or that one's diathermy is becoming too heavy-handed. These advantages are of course lost under general anaesthesia.

Smoking and Bronchial Carcinoma

Dr. LENNOX JOHNSTON (Wallasey, Cheshire) writes: Few, if any, non-smokers who have examined Dr. R. Doll's comprehensive study of the aetiology of bronchial carcinoma (*Journal*, September 5, p. 521) will be in any doubt that tobacco smoking is the main predisposing cause of this affection. But some 90% of our profession are smokers, and most smokers are under strong, unreasoning (pharmacological) compulsion to go on smoking whether it predisposes to bronchial carcinoma or not. Despite appearances to the contrary, I am convinced, as a result of my personal interrogation of thousands of smokers, that most smokers wish to stop smoking, and this wish must have been considerably strengthened by the findings of Wynder and Graham (*J. Amer. med. Ass.*, 1950, **143**, 329), Doll and Hill (*British Medical Journal*, 1950, **2**, 739), and others. Yet so much more immediate and compelling is the smoker's wish to appease his craving for tobacco and be rid of disagreeable feelings of tobacco deprivation that his wish to stop smoking is seldom effectively expressed—in non-smoking. How can smokers be helped to express effectively their wish to stop smoking? Only, I fear, by strengthening this wish by patient and, when necessary, pointed re-education and persuasion, until it becomes so strong that its expression in non-smoking cannot be denied.

Obituary

Sir EWEN MACLEAN, M.D., F.R.C.P., F.R.C.O.G.

As briefly announced in our last issue, Sir Ewen Maclean, Past President of the British Medical Association and formerly Chairman of the Representative Body, died at his home at Cardiff on October 13, only two days before his 88th birthday.

Ewen John Maclean was born on October 15, 1865, the second son of John Maclean, of Carmarthen. His brother, the late Sir Donald Maclean, was for many years a prominent figure in national politics, and at the time of his death in 1932 President of the Board of Education. Ewen Maclean was educated at Haverfordwest and Carmarthen grammar schools, and afterwards went to the University of Edinburgh, where he graduated M.B., C.M., with honours, in 1889, proceeding to the M.D., again with honours, in 1891. At Edinburgh he came under the religious influence of Henry Drummond, who at that time had a large following among young university men, and the impression on Ewen Maclean's character was an abiding one. He was elected M.R.C.P. in 1896, becoming a Fellow in 1922, and a Fellow of the Royal Society of Edinburgh as long ago as 1899.

[*Western Mail and Echo, Ltd., Cardiff*

After a term as house-surgeon at the Bristol Hospital for Women and Children he was appointed registrar to the Chelsea Hospital for Women and there started his life's work in obstetrics and gynaecology. On returning to his native Wales he practised as an obstetric physician in Cardiff and in 1901 was appointed to the staff of the Cardiff Royal Infirmary, where for many years he was senior gynaecologist, retiring in 1931 and becoming honorary consultant. On the creation of the Welsh National School of Medicine in the University of Wales in 1921 he was appointed professor of obstetrics and gynaecology, a post which he occupied for ten years. On his retirement he was elected emeritus professor. His distinction in his special field was recognized by his appointment as examiner in midwifery and diseases of women to the Central Midwives Board, the Conjoint Board of England, and Bristol and Liverpool Universities. He took a large share in the formation of the British (now Royal) College of Obstetricians and Gynaecologists, of which he was President from 1935 to 1938, and an original member of its council and a vice-president. He had also held the chair of the Section of Obstetrics and Gynaecology of the Royal Society of Medicine, and in 1922 he was president of the same Section at the Annual Meeting of the British Medical Association at Glasgow; he also served as a secretary of the Section in 1903 and as a vice-president in 1909 and 1930. He made many contributions on his own subject to medical publications, among which may be mentioned his paper on "Tuberculous Infection of the Female Genitalia" in the *Encyclopaedia of Midwifery and Diseases of Women*, an Oxford Medical Publication, in 1921, and in this *Journal*, on "The Remote Effects of Puerperal Sepsis," in 1935. During the war of 1914–18 he was officer commanding the Welsh Division of the 3rd West General Hospital and the Eaton Hall Officers Military Hospital at Chester. He was made lieutenant-colonel, R.A.M.C., in 1918.

In other fields also Ewen Maclean did good service. For many years he was a member of the Medical Advisory Committee of the Ministry of Health and chairman of the Welsh Consultative Council. He was an original member of the board of governors of the United Cardiff Hospitals under the National Health Service Act, serving in this capacity until shortly before his death. In the British Medical Association he provided the only instance of a Chairman of the Representative Body becoming President. His chairmanship was from 1910 to 1912, the stormy period which saw the introduction of the National Insurance Bill. Maclean was chairman of the Special Representative Meeting, at which Mr. Lloyd George was present, a month after the Bill was introduced. During the course of that struggle nine Representative Meetings were held, all of them concerned, wholly or mainly, with this new legislation. It was Ewen Maclean, along with Dr. J. A. Macdonald and Sir Jenner Verrall, who bore the chief burden of responsibility, and inevitably some of the ill-feeling and heartburning of the time attached itself, however undeservedly, to the man in the chair. Macdonald and Verrall weathered the long storm, but Maclean, like Victor Horsley, disappeared from the centre of B.M.A. affairs, and few thought he would ever come back.

It is doubtful whether Maclean, with his polite, fastidious manner, was quite happy in executive chairs or in conducting large controversial assemblies. But he was excellently equipped for the more ornamental tasks of President. In 1928, when the Association met for its Annual Meeting in his own city of Cardiff, he was chosen as President, and many will remember with what grace and success he carried through the social and other occasions of a memorable meeting. His address

was in part a review of ancient Cymric medicine, which revealed him as a good teller of folk-tale, and in part a retrospect and prospect of modern medicine, which revealed him as a statesman and prophet. No sooner was his presidential year over and the past-presidential badge—his own gift to the Association—on his shoulders than he was on his way to Australia, where he addressed the Australasian Medical Congress and laid the foundation stone of the new B.M.A. House in Sydney. He touched at many places on the outward and return journey, and received many interesting impressions of B.M.A. activity overseas. One thing which he came back to advocate was the need for more postgraduate study facilities for medical visitors to this country from the Dominions and Colonies, and he did his best to bring this about. Later he published an account of his journey under the title, *A B.M.A. Odyssey Round the World in 140 Days.* He again visited Australia in 1935, in which year the B.M.A. held its Annual Meeting at Melbourne, and during the course of that Meeting he received the honorary degree of M.D. of the University of Melbourne.

It was a joy to him to come back into the inner councils of the Association and to find three or four senior members with whom he had been associated in earlier and more stormy years. After his term of office as President he remained on the Council until 1943, and carried out much useful work, particularly on the Science and Ethical Committees and on the special committees set up to deal with medical education, the organization of the profession in India, the Indian Medical Service, and the medical aspects of abortion, among other subjects. He was chairman of the committee on the causation of puerperal morbidity and mortality, which reported in 1928. His membership of the Welsh Committee extended over a period of 25 years. Although a specialist, he was interested in —and had great knowledge of—the conditions of general practice, particularly contract practice in South Wales. In addition to his work for Cardiff Royal Infirmary, he was on the consulting staff of the Llandough Hospital, Cardiff, the Welsh National Memorial Association, and Porth, Mountain Ash, and Pontypridd Cottage Hospitals. He was for 20 years chairman of the Cardiff Insurance Committee. He was honorary secretary of the Cardiff Division of the B.M.A. from 1904 to 1907, chairman in 1912, and its Representative in the Representative Body from 1906 to 1913.

Sir Ewen Maclean—he was created a knight in 1923 —was elected a Vice-President of the British Medical Association in 1930. He was admitted to the Honorary Fellowship of the American College of Surgeons in 1926 and of the Royal College of Obstetricians and Gynaecologists in 1948, and he received the honorary degrees of D.Sc., Manchester, in 1929; LL.D., Edinburgh, in 1933; and LL.D., Wales, in 1947; in addition to the Melbourne degree mentioned above. He was a J.P. for the City of Cardiff and a Deputy Lieutenant for the County of Glamorgan, and was greatly esteemed by his fellow citizens of Cardiff. In the last war he was inspector of hospitals for Wales for the Red Cross and St. John War Organization. Maclean was a bachelor, and many members of the B.M.A. will recall how graciously his sister, Miss Agnes Maclean, who survives him, acted as hostess for him on public occasions.

We are indebted to Dr. Alfred Cox for the following appreciation: I wish to pay a heartfelt tribute to the memory of my dear old friend Ewen Maclean. I suppose he is not even a name to many readers of our *Journal*, but to his contemporaries and associates during a very difficult episode in B.M.A. history he is an honoured and distinguished figure. Your obituary notice records his many professional distinctions and his outstanding services to our Association, but I wish particularly to stress what he did in the great struggle over the old National Health Insurance system. He was Chairman of the Representative Body at the time, and together with J. A. Macdonald, Chairman of Council, led all the deputations to Mr. Lloyd George which argued the B.M.A. case. This he did in a masterly and persuasive way which culminated in the historic visit of Mr. Lloyd George to a meeting of the Representative Body. Nobody could have been more courteous—or more firm—and Maclean's management of that meeting was one of the finest things of the kind that I remember. But Maclean had a brother who was a prominent Liberal M.P. and an intimate friend of Lloyd George. This fact was used by a party of diehards in the Association to cast suspicion on Maclean's loyalty to the B.M.A. policy, and eventually their attitude convinced Maclean that it would be better in the interests of the Association that he should cease to take any active part in these negotiations, and he resigned his chairmanship. When he announced his intention the meeting rose and sang, "Will ye no come back again," but the diehards rejoiced. This episode hurt Maclean very much, but he was, and always continued to be, a loyal member of the Association. He had his revenge when his local colleagues chose him as President-elect for the Cardiff meeting in 1928, a position he filled with great credit to himself and particular pleasure to those of us who remembered the earlier episode. Nobody could meet Maclean without being impressed by his courtesy and dignity, which did not conceal from his friends a very kindly heart. There are not many privileges for old age, but I count it as one of my greatest to have been a friend and a colleague of Ewen Maclean.

Professor Gilbert I. Strachan has kindly sent us the following appreciation: Sir Ewen Maclean was the doyen of the profession in South Wales and of his specialty in the country generally. In 1901 he was appointed the first honorary gynaecologist to Cardiff Infirmary, later Cardiff Royal Infirmary, and he was the pioneer of obstetrics and gynaecology in South Wales. He built up a large private and hospital practice, and impressed both academic and local authorities with the importance of this subject, especially in relation to maternal mortality and to maternity and child welfare. As a clinician he was conscientious, thorough, and conservative, while his teaching was clear and to the point. His ability to recall incidents in his vast clinical experience and to deduce general principles from these added to the weight of his instruction, while his long-headed sagacity in surveying the various aspects of a difficult case was illuminating.

In the early formative years of the British (now Royal) College of Obstetricians and Gynaecologists his wise counsel and far-seeing wisdom were of the utmost value in the guidance of affairs, and he was largely responsible for the creation of the firm foundations from which the College has grown to its present position of importance.

Sir Ewen Maclean was one of the old school, but he was one of the best examples of that school, and his death severs one of the few remaining links with his generation. He witnessed the growth and development of modern obstetrics and gynaecology, and was always alive to the significance of each advance. Personally he was one of the most charming of men, kindly, urbane, and patient, while he was a finished orator and a forceful and convincing debater. His ethics and his rules of social conduct were rigid, and he looked for similar qualities in those with whom he worked. It was a pleasure to work with such a loyal and delightful colleague, and those of us who will not again see his tall and distinguished figure will for long mourn a staunch friend and an outstanding public personality.

For the last few years his health was poor, and he was confined either to his bed or to his bedroom, but he main-

tained his keen interest in professional and local affairs to the end. To his sister, who looked after him so sedulously in his later years, the deep sympathy of a vast number of friends will be extended.

J. H. BADCOCK, F.R.C.S., F.D.S.

By the death of Mr. J. H. Badcock at Malvern on September 23 in his 90th year the dental profession has lost almost the last of that band of teachers who, at the beginning of the century, did so much to raise the standard of British dentistry.

John Henry Badcock was born at New Barnet on March 7, 1864, and was educated at University College School at a time when dental students, much to their advantage, served an apprenticeship with a dentist to learn certain technical details of their work. After employment in that capacity Badcock went on to the London School of Dentistry (now the Royal Dental Hospital) and took the L.D.S. in 1887. He next studied medicine at Charing Cross Hospital and obtained the diplomas of M.R.C.S., L.R.C.P. in 1890. He became a Fellow of the Royal College of Surgeons of England, as a Member of more than twenty years' standing, in 1932, and he was elected a Fellow in Dental Surgery by the College in 1947. After qualification as a dentist Badcock established himself in Harley Street, where he practised for nearly fifty years until he retired in 1936. From 1891 to 1904 he held the appointments of dental surgeon to Guy's Hospital and lecturer on operative dental surgery in the dental school of the hospital. His skill in all departments of dentistry was of the highest order, and he had a wide outlook on scientific and especially medical fields. He was one of the finest exponents of the now almost forgotten art of cohesive gold filling, which has more than an antiquarian interest, because the scrupulous attention to detail, the judgment, and the great skill that are necessary to learn and to practise it laid the foundation of modern precision dental technique. Many of his students, now elderly men themselves, have good cause to remember him as a teacher and for his example, which encouraged them to try to attain the highest ideals of good service to their patients. He had a most charming and kindly personality and was an artist to the finger-tips.

During the first world war Badcock did valuable work as consulting dental surgeon to the 1st London General Hospital in connexion with the treatment of jaw injuries in German prisoners of war, and for a time he was professor of dental surgery at the Royal Army Medical College, Millbank. He was one of the founders of the British Society for the Study of Orthodontics and was its first president in 1908. He was honorary treasurer of the British Dental Association from 1919 to 1924 and president in 1925. He was also president of the odontology section of the Royal Society of Medicine in 1917 and president of the International Orthodontic Congress in 1931. A member of the British Medical Association for sixty-two years, he served on the Ministry of Health Committee of the Association from 1919 to 1921 and on the Insurance Acts Royal Commission special committee from 1924 to 1927. In his earlier days his chief interests outside his profession were boating and mountaineering.—J. B. P.

We are indebted to Mr. N. J. Ainsworth for the following appreciation:

With the death of John Henry Badcock the dental profession has lost the last remaining member of that group of great dental surgeons and teachers who could fairly claim specialist rank in every branch of dental science as it was practised in the early part of this century. Modern advances in knowledge and elaboration of technique have, as in all domains of surgery, made this impossible to-day, but in his day there was no difficult case which could not be referred for his opinion or treatment with the assurance that there was no higher court of appeal.

Notwithstanding his proficiency in technique, Badcock's most lasting mark on the practice of dentistry will have probably been made by his advocacy, to the hundreds of Guy's students to whom he taught operative dental surgery between 1893 and 1904, of the art of gentleness and the avoidance of pain. This was before the introduction of local analgesia, when pain was to many patients and only too many dentists synonymous with good work. Pain, it was true, was often unavoidable, but it was his gospel that all possible skill should be directed to minimizing it short of loss of efficiency.

A factual review of his life is impressive. His parents were not well off. His education at University College School was followed by apprenticeship to a qualified dental surgeon —the customary procedure in those days—and from this he proceeded to a distinguished student career at the London School of Dental Surgery. He carried off most of the prizes and scholarships available in spite of the competition of men whose names have since become famous in the profession. An assistantship in a Harley Street practice was combined with part-time medical study for his Conjoint diploma, and within three years of qualifying he was elected to Guy's Hospital dental staff as assistant surgeon and shortly afterwards as lecturer in operative dental surgery. In 1894 he was appointed honorary dental surgeon, but resigned both this post and the lectureship in 1904 on his marriage. Until then he had made a point of reading every dental journal available in English—a less formidable task, it is true, than nowadays—but he felt that marriage brought home responsibilities, and, as he has often explained, "I felt that I had delivered my message and should make way for others."

He held strong views on his duty to those less fortunate, and carried them out by private generosity and many years of service as chairman of the British Dental Association Benevolent Fund, which he always had much at heart. Surprisingly, he found time for a wide range of other activities. He was one of the first to ski in Switzerland, having acquired a pair of skis in Norway, and he traversed most of the waterways of France, Belgium, and Holland by canoe or yacht. Cruising was the chief hobby of his middle years, and his auxiliary-engined cruiser knew all the best reaches of the Thames and much of the south and east coasts. In old age, when handling a boat became too much of a strain, he still tried to make a yearly pilgrimage to his beloved river from his Suffolk home. He was a lover and tasteful collector of beautiful things, with a strong bias towards Chinese and Japanese art, and his home was always a delight to visit, both for its treasures and for the pleasure of his conversation and gentle humour. He was fortunate, as were his family and friends, in that he retained his mental powers and his physical senses unimpaired until his death.

T. A. MALLOCH, M.D., F.R.C.P.

Dr. Archibald Malloch, a former librarian of the New York Academy of Medicine, died at his home, White Plains, New York, on September 19. Thomas Archibald Malloch was born at Hamilton, Ontario, in 1887 and was educated at Queen's University, Kingston, and McGill University, where he graduated M.D., C.M. in 1913. For a short time he was assistant physician to the Royal Victoria Hospital, Montreal. During the first world war he served with the Canadian Forces in Europe and remained to take his M.R.C.P. in 1919. He was elected F.R.C.P. in 1930.

His lifelong friendship with Osler was no doubt responsible for developing Malloch's interest in medical history and books, and it was at Osler's suggestion that he wrote his delightful biography, *Finch and Baines, a Seventeenth Century Friendship*, in 1917. He published a life of Harvey in 1929 and in 1937 he edited a reprint of John Caius's classic on the sweating sickness. His biography of J. B. MacCallum, the physiologist, who died in 1906 at the early age of 30, appeared in 1938.

Malloch was appointed librarian of the New York Academy of Medicine in 1925. Here he paid particular attention to building up a magnificent historical collection. He retired in 1949. He took an active part in medical librarianship in North America, being elected president of the Medical Library Association in 1928. He joined the British Medical Association in 1923 and was vice-president of the Section of the History of Medicine at the Annual Meeting in London, in 1932. He was appointed FitzPatrick Lecturer at the Royal College of Physicians in 1939, but his lectures entitled "Medical Interchange Between the British Isles and America Before 1801" were not delivered owing to the outbreak of war: they were published by the College in 1946.

Sir Arthur S. MacNalty writes: Will you allow me to pay a brief tribute to Archibald Malloch? The son of Osler's old friend, Dr. A. E. Malloch, he served as a medical officer in the first world war and spent his leaves with the Oslers at Norham Gardens, Oxford, where I first met him. While in charge of a hospital at Burley-on-the-Hill, the home of the Finches, he wrote his excellent monograph on Finch and Baines, "the David and Jonathan of the profession in the seventeenth century," which established his reputation as a medical historian. He did this at Osler's suggestion, worked in the Bodleian, and discovered many interesting facts about their historic friendship.

In 1918–19 Malloch studied in France and England the pandemic of influenza which was then raging. He showed his notes to Sir William, who was impressed by them and suggested to Malloch and myself that we should collaborate in an article on influenza for the *Nelson Loose-leaf System of Medicine*, Malloch writing the medicine and pathology—he did it extremely well—and I dealing with the history of influenza, its epidemiology and vaccine therapy. Soon afterwards Osler was stricken by this malady, and during the final stages, Archie, like a true friend, kept me constantly informed of the patient's condition. Later, I often met Archie at Oxford, where he was helping Dr. Francis with the *Bibliotheca Osleriana*. When I was in New York in 1939 he showed me over the library of the New York Academy of Medicine, to which the rest of his life was devoted, and afterwards we continued to correspond frequently. His FitzPatrick Lectures to the Royal College of Physicians are scholarly and of value. His later years were a struggle against ill-health. Had it not been for this and for his self-sacrifice of time to help others, he would have written more. But he did enough in his noble and studious life to ensure that his memory will not be forgotten by students of medical history.

R. H. BURNE, M.A., F.R.S.

Mr. R. H. Burne, sometime physiological curator of the Hunterian Museum of the Royal College of Surgeons of England, died on October 9 at the age of 85.

Richard Higgins Burne was born in London on April 5, 1868, and was educated at Winchester and Oriel College, Oxford, where he took third-class honours in natural science in 1889. In 1892, after two years' study at the Royal College of Science in South Kensington, he was appointed anatomical assistant in the museum at the Royal College of Surgeons, becoming assistant conservator in 1908. From 1912 to 1934, when he retired, he was in charge of the physiological section of the museum. He was an extremely skilful dissector, and his contributions to biology were mainly in the field of comparative anatomy. In 1927 he was elected F.R.S. The Royal College of Surgeons awarded him the honorary medal of the College in 1925 for distinguished services, and he was elected a trustee of the Hunterian Collection in 1937.

Mr. Burne was a widower, and is survived by his son and daughter.

We are greatly indebted to Sir Arthur Keith, F.R.S., for the following appreciation: During my years at the Royal College of Surgeons (1908–33) it was my good fortune to have as a colleague the late Mr. Richard Burne. The success of our partnership was due more to his qualities than to mine, for never was a man less self-seeking; it seemed to come naturally to him to think of what he could give to life, not what he could get from it. He was a cultured man, one who had undergone the discipline of Winchester and Oxford, but his modesty, just as was his uncommon ability, was innate. He was brought up in easy financial circumstances, and resolved to make the subject which most appealed to him—biology—his life's work. He worked first at the Royal College of Science, South Kensington, under Professor G. B. Howes, and then under Professor Charles Stewart at the Royal College of Surgeons; under these masters he developed a marvellous skill in the dissection of the most fragile of structures. It was this gift of dissection, united to a wide first-hand knowledge of comparative anatomy, that made it possible for him to do so much for the most important of all parts of the Hunterian Collection—the physiological series. Like Hunter, Burne published his discoveries on the shelves of the Museum. Some, to be sure, he contributed to the proceedings of the Zoological and Royal Societies. Alas, so much of his work was blotted out by the bombs of the enemy.

Dr. Nest Kahan died in St. James's Hospital, Balham, on September 16, following an operation, at the age of 42. Born on April 17, 1911, the eldest daughter of Mr. Owen Thomas, Nest Kahan received her medical training at the Royal Free Hospital, London, qualifying M.R.C.S., L.R.C.P. in 1934. Three years later she obtained the London degrees of M.B., B.S. For the greater part of the last war she held an appointment as physician at the E.M.S. Southern Hospital, Dartford. On relinquishing this in 1947 her interests turned to psychiatry, but in the following year her career was interrupted for operative treatment of the condition which eventually caused her death. In 1949 she was appointed to Horton Hospital, where for most of her period of service she held the position of registrar. Last year she obtained the Diploma in Psychological Medicine; six years earlier she took the D.C.H. Dr. Kahan was a person of the highest integrity, and her untimely death has undoubtedly cut short a career in psychiatry which would have been an outstanding success. She was a shrewd and careful clinician, and her experience and special qualifications were found to be invaluable during the difficult period when Horton Hospital was reverting to its original psychiatric function. She will be long remembered for her happy relationship with both staff and patients, and for her humane attitude to their divers problems. She was clearly conscious of the uncertainty of the outcome of her original illness, but she did not allow this to cast a shadow over her day-to-day relationships. There were times during the past two years when she suffered great pain. Her steadfastness, courage, and devotion to duty under these circumstances were the admiration of all who shared her secret. It can truly be said that the ability to display such courage is given to few of us. She will be sadly missed by both the medical and the nursing staff of Horton Hospital. Deep sympathy will be felt for her husband, Dr. Alexander Kahan, and for her daughter and son.—J. H. W.

Medico-Legal

DEFECTIVE ETHER VAPORIZER

[From our Medico-Legal Correspondent]

A married woman aged 34 was admitted on August 11 to the Royal Hospital, Great Western Road, Gloucester, for a total hysterectomy. The operation was performed on August 13, anaesthesia being by cyclopropane and ether.

The anaesthetic was begun at 9.50 a.m. and the abdomen was opened at 10.15, when the patient's condition was excellent, her pulse rate being 84. At 10.20 there was a slight deterioration in her condition, the pulse rate rising to 96. At 10.23 she suddenly collapsed, with a bad colour, an imperceptible pulse, and no voluntary respiration. After 13 minutes of resuscitative treatment the action of her heart was restored, and at 10.45 voluntary respiration started again. But she did not regain consciousness, and died early in the morning of August 16.

When the patient first collapsed the anaesthetic circuit was flushed with oxygen, which revealed the presence of liquid ether in the afferent tube. As soon as possible after the emergency the anaesthetist examined the machine with the coroner's officer, and formed the opinion that the wick of the ether vaporizer had, because of its texture and the size of its mesh, become relatively impermeable to the circulating gases and had functioned as a cylinder up which liquid ether had been sucked from the bottom of the bottle into the circuit.

At the inquest held before the Gloucester city coroner and a jury on August 18 and 31 the evidence was that the standard wide-mesh ether wick, as designed and manufactured for the machine and supplied with it, was missing, and a piece of heavy material of double thickness and of close texture had been substituted. The vaporizer was of the surface type, and the incoming gases, mixed with the patient's exhaled gases, pass into the ether tube above the ether level and pass out through the meshes of the wick in which they become etherized. The gases, if unable to pass through the wick, would force liquid ether up the delivery half of the centre tube into the unit, and this is what happened when the substituted wick was used on test. The turbulence created in the liquid ether on test was both visible and audible.

The cause of death was recorded as irreversible anoxia with pneumonia and cerebral oedema, the sequel to the delivery of liquid ether instead of vapour during anaesthesia.

SENTENCE REDUCED ON APPEAL

[From Our Medico-Legal Correspondent]

On October 13 the Justiciary Court of Appeal in Edinburgh reduced a sentence of 60 days' imprisonment on Dr. John Joseph Flanigan, of Coatbridge, to a fine of £25 with the alternative of three months' imprisonment. Dr. Flanigan on August 3 had pleaded guilty at Airdrie Sheriff Court to a charge of defrauding the Lanarkshire Executive Council of £43 15s.[1]

In his judgment the Lord Justice General Lord Cooper said that the circumstances which he thought justified the court in holding that the original sentence of 60 days' imprisonment without the option of a fine to be in law "oppressive" were the professional zeal of Dr. Flanigan, the fact that he had made complete restoration of the money improperly obtained by him from the authorities, and the background of difficulty under which he had been working. He added that it must not be assumed that, if further cases arose, frauds on the National Health Service would be dealt with other than severely.

[1] *British Medical Journal*, August 15, p. 399.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **October 3** (No. 39) and corresponding week 1952.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1953					1952				
	Eng. & Wales	Lond	Scot.	N. Ire	Eire	Eng. & Wales	Lond	Scot.	N. Ire	Eire
Diphtheria	24	3	7	0		15	4	2	1	1
Dysentery	212	29	139	0	2	123	44	66	2	2
Encephalitis, acute	7	0	0	0		3	2	0	0	
Enteric fever:										
Typhoid	10	5	0	1	3	3	0	0	0	1
Paratyphoid	16	1	1	0	1	31	1	0	0	
Food-poisoning	260	16		0		137	17		1	
Infective enteritis or diarrhoea under 2 years				19	48				21	35
Measles*	621	9	69	17	29	3,272	354	72	20	27
Meningococcal infection	22	2	11	0	2	21	2	14	0	1
Ophthalmia neonatorum	42	5	1	0		44	5	3	0	
Pneumonia†	322	16	109	5	2	316	22	181	3	
Poliomyelitis, acute:										
Paralytic	79	4	9	16	6	104	5	11	10	4
Non-paralytic	78	6				57	4			
Puerperal fever§	237	38	9	3		249	38	14	0	
Scarlet fever	992	61	194	38	62	1,164	129	242	17	75
Tuberculosis:										
Respiratory			126	27				133	30	
Non-respiratory			22	6				11	3	
Whooping-cough	2,292	142	224	26	47	1,258	81	66	24	57

DEATHS in Great Towns	1953					1952				
	Eng. & Wales	Lond.	Scot	N. Ire.	Eire	Eng. & Wales	Lond	Scot.	N. Ire	Eire
Diphtheria	0	0			0	0	0		0	0
Dysentery	0	0				0	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0				1	0		0	
Infective enteritis or diarrhoea under 2 years		3	1	0	2	7	0	1	1	2
Influenza	4	0		0	0	2	0		0	0
Measles		0			0		0		0	0
Meningococcal infection		0					0			
Pneumonia	135	18		6	5	161	22		10	2
Poliomyelitis, acute	6	0			0	6	0			0
Scarlet fever		0			0		0			0
Tuberculosis:										
Respiratory	84	11	7	3	1	66	11	13	3	6
Non-respiratory		0	3	0	2		0	1	0	1
Whooping-cough	1	0		0	0	3	0		1	0
Deaths 0–1 year	207	31	30	10	12	216	30	25	9	14
Deaths (excluding stillbirths)	4,495	606	509	87	141	4,365	674	522	103	159
LIVE BIRTHS	7,769	1189	854	199	385	7,621	1161	810	254	431
STILLBIRTHS	194	24	17			201	22	28		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

Poliomyelitis

Poliomyelitis notifications (uncorrected) in the week ending October 10 (40th week of the year) were as follows: paralytic, 107 (79); non-paralytic, 69 (78); total 176 (157). This is an increase of 19 compared with the previous week, the figures for which are in parentheses, but there is no reason to believe that the general downward trend will not quickly be resumed.

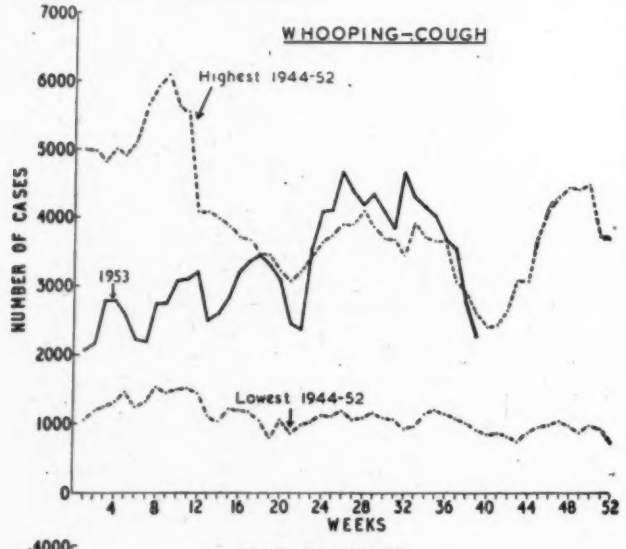
England and Wales Third Quarter

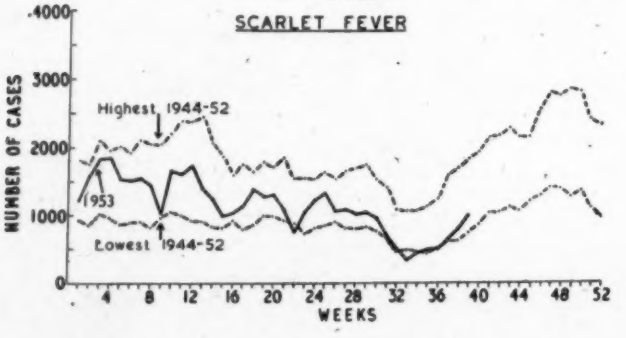
Provisional figures for England and Wales for the third quarter of this year show that the birth rate was higher and the stillbirth and infant mortality rates lower than the rates for the corresponding quarter of 1952 (*Weekly Return* No. 40). Live births numbered 172,976, representing a rate of 15.6 per 1,000 population; in the third quarters of both 1952 and 1951 the corresponding rate was 15.2. There were 3,709 stillbirths, representing a rate of 21.0 per 1,000 total live and stillbirths, compared with a rate of 21.6 in the corresponding quarter of 1952. The figures for the third quarter of 1938 were 6,072 and 37.0 respectively.

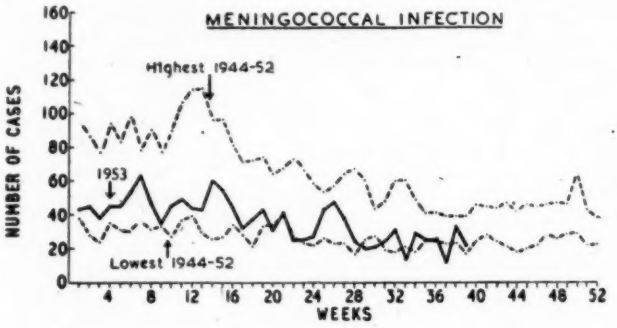
Deaths numbered 98,588, giving a rate of 8.9 per 1,000 population, compared with a rate of 8.9 in the third quarter of 1952 and of 9.1 in the third quarter of 1951. Deaths of children under 1 year of age numbered 3,832, or 22.2 per 1,000 related live births. The rate for the third quarter 1952 was 22.8; in the third quarter of 1938 the rate was 42.5.

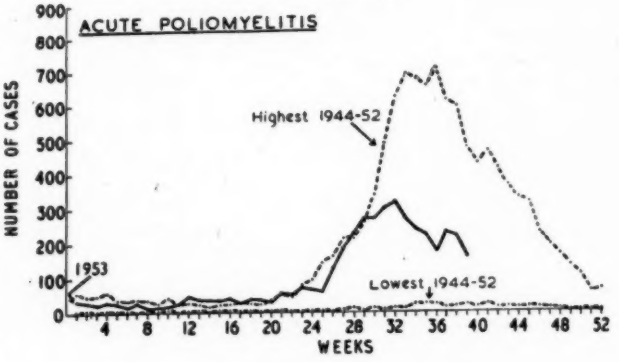
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1944–52 are shown thus - - - - - - -, the figures for 1953 thus ————. Except for the curves showing notifications in 1953, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

The largest variations in the trends of infectious diseases in England and Wales during the week ending October 3 were an increase of 206 for scarlet fever, from 786 to 992, and 129 for measles, from 492 to 621, and a decrease of 479 for whooping-cough, from 2,771 to 2,292.

Only small fluctuations were recorded in the local trends of scarlet fever. The largest was a rise of 47 in the number of notifications in Yorkshire West Riding, from 92 to 139. The number of notifications of whooping-cough have fallen steadily for the past seven weeks, and the incidence is now half what it was in mid-August. The largest falls during the week were 76 in Warwickshire, from 216 to 140, 52 in Lancashire, from 221 to 169, and 48 in London, from 190 to 142. The largest rise in the number of notifications of measles was 56 in Somersetshire, from 13 to 69, and was due to an outbreak in Taunton, R.D. 24 cases of diphtheria were notified, and these were 5 fewer than in the preceding week. The largest variations in the local returns were a fall in Lancashire from 9 to 4 and a rise in Staffordshire from 4 to 7. The 7 cases in Staffordshire were notified in Coseley U.D. Diphtheria has been running at a very similar level to that of last year. During the past 10 weeks 199 cases have been notified compared with 206 for the corresponding period of last year. 5 of the 10 cases of typhoid fever were notified in London from five boroughs.

157 cases of acute poliomyelitis were notified during the week. These were 40 fewer for paralytic and 21 fewer for non-paralytic than in the preceding week. The chief centres of infection were Lancashire 19 (Liverpool C.B. 4), Warwickshire 18 (Coventry C.B. 8, Birmingham C.B. 5), Glamorganshire 11 (Cardiff C.B. 5, Penarth U.D. 4), London 10, Devonshire 9 (Plympton St. Mary R.D. 5), Yorkshire West Riding 9, Northamptonshire 8 (Kettering M.B. 5).

212 cases of dysentery were notified, being 51 fewer than in the preceding week. The largest returns were Lancashire 45 (Liverpool C.B. 11), London 29 (Islington 8), Middlesex 27 (Tottenham M.B. 8), and Yorkshire West Riding 19.

Of the 139 cases of dysentery in Scotland, 90 were notified in Glasgow and 20 in Edinburgh.

Week Ending October 10

The notifications of infectious diseases in England and Wales during the week included scarlet fever 986, whooping-cough 2,395, diphtheria 20, measles 691, dysentery 267, paratyphoid fever 13, and typhoid fever 4.

Medical News

Harveian Oration.—Dr. George Graham, consulting physician to St. Bartholomew's Hospital, delivered this year's Harveian Oration before the Royal College of Physicians on October 16. He took as his subject "The Value of Physiology in Medicine." It is hoped to publish the Oration in the *Journal*.

Physiology Laboratory at Oxford.—This term, work is starting in the new University Laboratory of Physiology. The old laboratory was built, after much opposition, in 1885; since then it has grown tortuously on a restricted site to meet the needs of the Honour School of Physiology and of the researches of Burdon-Sanderson, Gotch, Haldane, Sherrington, J. Mellanby, and their co-workers. The new laboratory is a long, narrow four-storied building with a south frontage towards the Biochemical Department and overlooking the main science area east of the Museum. The north side faces the Parks. The spacious entrance leads to a big lecture theatre. There are also a small theatre and a demonstration theatre. Off the main corridors are large airy classrooms with their preparation rooms and small specialized teaching-rooms. Parts of the building contain the teaching staff and research workers' rooms, some already equipped for the study of electrophysiology, histology, respiration, and chemical physiology, others capable of adaptation as the needs of the future arise. The research library overlooks the Parks. The workshops have been in use for some time, much of the new apparatus for the classrooms having been made in them. The fourth story is set back and contains animal quarters and a small operating theatre; outside is a long expanse of flat roof providing an extra classroom for the study of respiration and exercise. The building was planned by Messrs. Lanchester and Lodge with the co-operation of Professor E. G. T. Liddell, Waynflete Professor of Physiology.

Royal College of Obstetricians and Gynaecologists.—A very large company of Fellows and Members and their guests attended the annual dinner, and later danced, at the Dorchester Hotel, London, on October 16. The guests, in fact, of whom many were ladies, handsomely outnumbered their hosts; they included the Minister of Health, the Lieutenant-Governor of Victoria, Australia, and the presidents of medical colleges and societies. Mr. Arthur Gemmell, President of the Royal College of Obstetricians and Gynaecologists, was in the chair. After the Loyal Toast Sir Francis Walshe proposed the toast of the College. Up and down the country, he said, enshrined in marble in the parish churches was the evidence of what childbirth had been like in the past. So often one saw on a tomb the figure of a young mother with her child in her arms. In those days death in childbed was a commonplace. Now, thanks a great deal to the work of the obstetricians, this had been changed. Replying, the chairman spoke of the future of the College. It was not a rich college, but the occasion of its silver jubilee next year would be taken to re-launch the appeal, directed by Sir Ronald Weeks, for funds for a new building. No longer was the "semi-detached villa round the corner" adequate for the College's purposes. It was intended to concentrate on a really representative museum of obstetrical and gynaecological specimens—he appealed to Fellows and Members to send theirs to the College—and on a historical library of their subject. In the course of his speech Mr. Gemmell stressed the Commonwealth nature of the College, a fact that had been specially brought home to him during this Coronation year. Professor J. F. Cunningham, of Dublin, proposed "The Guests," mentioning many by name. He noted with particular pleasure the presence of Sir Arthur Sims, donor of the Commonwealth Travelling Professorship. He warmly commended the College's appeal to its Fellows, quoting Virgil's boat-racing slogan, *Possunt quia posse videntur*. On behalf of the guests, replies were made by the Minister of Health and Sir Edmund Herring, Lieutenant-Governor of Victoria. Mr. Macleod, having disarmingly claimed that the toast was an impossible one to answer, proceeded to make the speech of the evening. As an Australian had once said to him, "In London there are more speeches to the square meal than anywhere else in the world." He promised every assistance in his power to the College's appeal, and condemned as "rather silly" the tradition that Ministers should keep aloof from that kind of thing. The future of the College was obviously of the greatest interest to a Minister of Health. Sir Edmund Herring, as an Australian, was very glad to underline what had been said about the Commonwealth attachments of the College. He urged more people from Britain to visit the Dominions "to see what they are like and meet the people who live there." Only in that way could the Commonwealth family be kept truly together. After the speeches the room was cleared and there was dancing.

Bisset Hawkins Medal.—Dr. W. N. Pickles, of Aysgarth, Yorkshire, received the Bisset Hawkins Medal of the Royal College of Physicians at the Harveian Oration on October 16. In the citation his epidemiological studies receive special acclaim, particularly those of infective hepatitis and epidemic myalgia. "But," continues the citation, "perhaps his outstanding achievement is the demonstration that scientific observation and deduction are not only possible under the pressure of a busy general practice, but are a constant stimulus to the quality of the service that the general practitioner can give to his patients." The Bisset Hawkins Medal was founded in 1896 by Captain Edward Wilmot Williams with a gift of £1,000 to the College. It is awarded for notable work in the field of public health. The last recipient was Sir Wilson Jameson.

Medical Statistics.—The monthly meetings of the Study Circle on Medical Statistics, which are normally held in the Westminster Medical School, may be of interest to many besides statisticians, and all doctors are invited. Further information may be obtained from the hon. secretary, Mr. M. P. Curwen, St. Bartholomew's Hospital, London, E.C.1.

French Prize for Medical Films.—*Presse Médicale*, the French medical journal, offers a prize of 100,000 frs. (about £100) for the best 16 mm. medical or surgical teaching film made by an amateur. No film made or subsidized by a commercial firm is eligible. Further information may be obtained from *Presse Médicale*, 120, Boulevard Saint-Germain, Paris, 6. The last date for entries is February 28, 1954.

New Professor at Dublin.—On October 8 Mr. John Seton Pringle was appointed Professor of Surgery in the Royal College of Surgeons in Ireland. Mr. Pringle is a son of Mr. Seton S. Pringle, a former President of the College.

Faculty of Dental Surgery.—The Board of Faculty of Dental Surgery, Royal College of Surgeons of England, has elected Professor F. C. Wilkinson and Professor H. H. Stones as dean and vice-dean, respectively, of the Faculty.

Sir Sydney Smith has arrived in Ceylon, where he is acting as medico-legal consultant to the Government. The object of his visit is to reorganize the country's medico-legal services on modern lines.

Professor Joseph Trueta, Nuffield Professor of Orthopaedic Surgery at Oxford, has been created a Chevalier de la Légion d'Honneur by the French Government for his services to French wounded in Britain during the last world war.

Professor C. W. Asling, of the University of California, is coming with a Fulbright Award to work with Professor R. G. Harrison at Liverpool University on endocrinological factors in arthritis. Professor Asling will be in Britain for a year.

Dr. Otto Steinbrocker is to be the guest lecturer at the Empire Rheumatism Council's week-end course at the Arthur Stanley Institute, Middlesex Hospital, on November 13 and 14.

Mr. B. W. Rycroft has accepted an invitation from the Ophthalmological Society of South Africa to deliver a series of lectures on plastic surgery and the eye.

COMING EVENTS

Ciba Foundation Lecture.—Professor A. von Muralt, professor of physiology at Berne, will deliver the fifth Ciba Foundation Lecture at the Royal Society of Medicine at 5 p.m. on October 29. His subject will be "Neurophysiology: Old and New Facts and Theories." Dr. E. D. Adrian, O.M., P.R.S., will be in the chair. Admission is free, without ticket.

Social Psychiatry.—The third Conference on Social Psychiatry (under the auspices of the Institute of Social Psychiatry) will be held at B.M.A. House, Tavistock Square, London, W.C.1, on October 30 and 31. Further details may be obtained from the Institute, 9, Fellows Road, Hampstead, London, N.W.3.

Immunization in Young Children.—A conference on this subject will be held at the Highgate Wing of Whittington Hospital, Dartmouth Park Hill, London, N.19, on October 31 from 2.30 to 6 p.m. Dr. J. A. Scott will be in the chair, and papers will be read by Dr. W. C. Cockburn, Dr. S. King, and Dr. T. M. Pollock. Admission by ticket, obtainable from the Paediatric Department of Whittington Hospital.

British Medical Students' Association.—The annual general meeting will be held in Bristol from November 5 to 7. The annual ball will be held on November 6 at the Victoria Rooms, Bristol. Medical practitioners are cordially invited. Tickets, price one guinea (double), are obtainable from D. I. D. Hodge, c/o M.C.R., Bristol Royal Infirmary.

Empire Rheumatism Council Week-end Course.—The autumn week-end course of the Council will be held at the Arthur Stanley Institute, Middlesex Hospital, Peto Place, Marylebone Road, London, N.W.1, on November 13 and 14. The course will consist of lecture-demonstrations on various aspects of rheumatic diseases. The fee for the course is two guineas, and applications should be sent to the General Secretary, Empire Rheumatism Council, Tavistock House (North), Tavistock Square, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Applications should be made first to the institution concerned.

Saturday, October 24

OXFORD UNIVERSITY.—At Maternity Lecture Theatre, Radcliffe Infirmary, 9.15 a.m., Dr. T. R. C. Fraser: Radio-iodine in the Diagnosis and Treatment of Thyroid Disease.

Monday, October 26

●INSTITUTE OF CHILD HEALTH, Hospital for Sick Children.—5 p.m., Alex Simpson Smith Lecture for 1953 by Professor E. Husfeldt (Copenhagen): Hiatus Hernia in Adults and Children.

LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Heath Clark Lecture by Dr. Paul F. Russell (Rockefeller Foundation): Man's Mastery of Malaria—(1) The Unfolding of Malaria Aetiology.

MANCHESTER MEDICAL SOCIETY: SECTION OF ODONTOLOGY.—At Medical School, Manchester University, 5 p.m., Presidential address by Mr. Colin Cooke: Dentistry and the Social Services; 7 p.m., dinner. SECTION OF GENERAL PRACTICE.—At Medical School, Manchester University, 9 p.m., Dr. R. W. Fairbrother: Problems of Antibiotic Treatment in General Practice.

MEDICAL SOCIETY OF LONDON.—8.30 p.m., discussion to be introduced by Mr. H. J. Seddon and Mr. W. Ritchie Russell: Treatment of the Early Stages of Poliomyelitis.

●POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. C. C. Ungley: Role of Vitamin B_{12} and other Haemopoietic Factors in Megaloblastic Anaemias.

ROYAL EYE HOSPITAL.—5.30 p.m., Miss J. M. Dollar: Management of Cataract.

Tuesday, October 27

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. S. C. Gold: Allergy in Diseases of the Skin.

LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Heath Clark Lecture by Dr. Paul F. Russell (Rockefeller Foundation): Man's Mastery of Malaria—(2) The Unravelling of Malaria Therapy. At Birkbeck College, 6 p.m., Inaugural Lecture by Professor W. S. Bullough: History of Hormones.

MANCHESTER MEDICAL SOCIETY.—At Medical School, Manchester University, 4.30 p.m., Mr. R. L. Newell: The History of Urinary Calculi.

ROYAL STATISTICAL SOCIETY: STUDY CIRCLE ON MEDICAL STATISTICS.—At Westminster Medical School, 6 p.m., discussions: (1) Measures of Morbidity in the Field of Public Health; (2) Statistical Aspects of Disease Classification (Preliminary Report).

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Theatre, 5 p.m., Mr. D. H. MacLeod: Trial Labour.

SOUTH-WEST LONDON MEDICAL SOCIETY.—At Bolingbroke Hospital, 8.30 p.m., Mr. A. Lawrence Abel: Early Diagnosis of Malignant Disease.

Wednesday, October 28

BIRMINGHAM MEDICAL INSTITUTE: SECTION OF PSYCHIATRY.—6 p.m., lecture and film by Dr. E. J. M. Bowlby: A 2-Year-Old Goes to Hospital.

EDINBURGH CLINICAL CLUB.—At Royal Hospital for Sick Children, Edinburgh, 4 p.m., clinical meeting. Mr. A. B. Wallace: Treatment of Chronic Leg Ulcers.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. J. O. Oliver: Immunology.

INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. H. G. Hanley: Urological Problems in Pregnancy.

LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Heath Clark Lecture by Dr. Paul F. Russell (Rockefeller Foundation): Man's Mastery of Malaria—(3) The Development of Malaria Prophylaxis.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Professor G. F. Marrian, F.R.S.: Steroid Metabolism.

RENAL ASSOCIATION.—At Ciba Foundation, 4.30 p.m., discussion to be opened by Professor E. B. Verney, F.R.S., Dr. B. E. Miles, and Dr. A. A. G. Lewis: Emotion and Renal Function.

ROYAL EYE HOSPITAL.—8 p.m., Clinical Society Meeting. Mr. B. H. Dawson: Blood Supply of the Visual Pathway and its Clinical Aspects.

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Theatre, 5 p.m., lecture-demonstration by Dr. G. W. B. James: Psychological Medicine.

Thursday, October 29

CIBA FOUNDATION.—At Royal Society of Medicine, 5 p.m., 5th (Annual) Ciba Foundation Lecture by Professor A. von Muralt (Berne): Neurophysiology—Old and New Facts and Theories.

HONYMAN GILLESPIE LECTURE.—At University New Buildings, Edinburgh, 5 p.m., Dr. G. O. Horne: Effects of Environmental Heat.

●INSTITUTE OF CHILD HEALTH AND INSTITUTE OF NEUROLOGY.—At National Hospital, Queen Square, W.C., 5.30 p.m., Dr. Paul H. Sandifer: Cerebral Diplegia—Clinical Types, Diagnosis, and Treatment.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. W. Riddell: Diagnosis of Skin Infections Due to Pathogenic Fungi.

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Chelsea Hospital for Women, 3 p.m., Mr. A. A. Gemmell: Myomectomy.

LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Heath Clark Lecture by Dr. Paul F. Russell (Rockefeller Foundation): Man's Mastery of Malaria—(4) Some International Aspects of Malariology.

MANCHESTER MEDICAL SOCIETY: SECTION OF ANAESTHETICS.—At Medical School, Manchester University, 8 p.m., Presidential address by Dr. H. E. Pooler: Operation Child.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—3.30 p.m., Professor G. F. Marrian, F.R.S.: Steroid Metabolism.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Thomas Vicary Lecture by Sir Ernest Finch: The Forerunner.

ST. ANDREWS UNIVERSITY.—At Physiology Department, Dundee, 5 p.m., Dr. F. Avery Jones: Problem of Peptic Ulcer.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Dr. M. A. Partridge: psychiatry demonstration.

●WEST LONDON MEDICO-CHIRURGICAL SOCIETY.—At South Kensington Hotel, 7.30 for 7.45 p.m., dinner meeting. Presidential address: Featuring the Nose.

Friday, October 30

INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. S. C. Gold: Skin Testing.

KENT AND CANTERBURY HOSPITAL.—8 p.m., clinical meeting.

LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Heath Clark Lecture by Dr. Paul F. Russell (Rockefeller Foundation): Man's Mastery of Malaria—(5) Malaria and Society.

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES.—7.30 p.m., Dr. E. M. C. Dunlop and Mr. F. B. Zwink: Corneal Changes in Congenital Syphilis.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Professor G. F. Marrian, F.R.S.: Steroid Metabolism.

ROYAL COLLEGE OF SURGEONS OF ENGLAND: FACULTY OF ANAESTHETICS.—4.30 p.m., Frederic Hewitt Lecture by Dr. Frankis T. Evans: Freedoms of Anaesthesia.

ROYAL EYE HOSPITAL.—4.30 p.m., Mr. A. J. Cameron: Recent Advances in Cataract Surgery.

Saturday, October 31

ASSOCIATION OF CLINICAL BIOCHEMISTS (N.W. REGION).—At Department of Physiotherapy, Crumpsall Hospital, Manchester, 2 p.m., 6th scientific meeting.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Bagchi.—On October 5, 1953, to Eileen, wife of Dr. J. C. Bagchi, Bentley, Staffs, a daughter—Amanda.

DEATHS

Banks.—On September 26, 1953, at his home, 114, Castelnau, Barnes, London, S.W., James Reid Banks, M.B., B.S., aged 60.

Broom.—On September 26, 1953, at 204, Stockport Road, Marple, Cheshire, James Prowse Broom, M.B., Ch.B., D.P.H., formerly of The Sycamores, Old Trafford, Manchester.

Francis.—On October 5, 1953, in the Middlesex Hospital, London, W., John Emlyn Francis, M.D., M.R.C.P., D.P.H., D.C.H.

Grist.—On September 25, 1953, Guy Spencer Grist, L.M.S.S.A., of Horsley's Green, High Wycombe, Bucks.

Haythornthwaite.—On September 21, 1953, at The College, Durham, Edward Parker Haythornthwaite, L.R.C.P.&S.Ed., L.R.F.P.S., late of Rowrah, Cumberland.

Hutchison.—On September 29, 1953, at Jordans, Bucks, Alice Marion Hutchison, M.D., M.R.C.P., aged 79.

Macaulay.—On September 29, 1953, Bryce Johnston Macaulay, M.D., of 6, King's Drive, and Grosvenor House, Eastbourne, Sussex, aged 86.

Noy Scott.—On October 14, 1953, at Colebrook House, Plympton, South Devon, Anthony Noy Scott, L.M.S.S.A., aged 29.

Shone.—On September 24, 1953, at Royde House, Midvale Road, St. Helier, Jersey, Henry John Shone, M.B., B.C., aged 76.

Talbot.—On September 29, 1953, at Cheddleton Lodge, Prestwich, Manchester, Geoffrey Talbot, M.B., Ch.B.

Trotter.—On September 25, 1953, at Stonegate, Hunmanby, Yorks, Edward Trotter, M.B., F.R.C.S., formerly of Scholes, Holmfirth, Yorks.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Mixing Antibiotics in the Syringe

Q.—*Is there any objection, when more than one antibiotic is being given—for example, penicillin and streptomycin in peritonitis—to mixing them in the syringe? Which antibiotics are, pharmacologically speaking, compatible?*

A.—When solutions of penicillin and streptomycin (streptomycin-calcium chloride *B.P.*) are mixed no precipitation occurs, and there would seem to be no objection to mixing the two substances in the syringe. Such a method of administration would allow more flexibility in dosage than is afforded by the use of proprietary mixtures of fixed composition.

The question of combined chemotherapy of bacterial infections has recently been discussed in considerable detail by Professor L. P. Garrod.[1] Antibiotics can be divided into two groups. Members of the first group are bactericidal—for example, penicillin, streptomycin, and neomycin—and of the second group bacteriostatic—for example, aureomycin, terramycin, and chloramphenicol. Substances in the first group often potentiate one another. Combinations within the second group usually give additive effects. If, however, a member of the first group is combined with a member of the second group the bacteriostatic action of the latter may interfere with the bactericidal effect of the former, and the net result may be less than if either drug were used separately. These views are based largely on *in vitro* observations, but clinical experience in the treatment of both pneumococcal and meningococcal meningitis lends support to them. It would seem wise, therefore, to avoid such combinations until more clinical evidence in other conditions is available.

Reference

[1] *British Medical Journal*, 1953, **1**, 953.

Acute Mesenteric Lymphadenitis

Q.—*What are the aetiology and treatment of acute mesenteric lymphadenitis, and how may this condition be differentiated from early appendicitis?*

A.—The aetiology of acute non-specific lymphadenitis is unknown. The appearance of the glands at operation suggests an infective cause, and sometimes there is hyperaemia and thickening of the terminal ileum or of the appendix and caecum. Some authorities believe that mesenteric adenitis is due to a generalized virus infection, and the previous or simultaneous occurrence of upper respiratory tract infection has been held to substantiate this view. A recent history of sore throat is, however, not peculiar to a minority of cases of mesenteric adenitis and sometimes occurs with appendicitis too. Non-specific mesenteric lymphadenitis is not due to tuberculosis, although this diagnosis is wrongly made in a proportion of cases. While the appearance of the glands, and sometimes of the gut, is similar to that occasionally seen in early acute regional ileitis (Crohn's disease), there is no established relationship between the two conditions.

Differentiation of early acute appendicitis and non-specific mesenteric lymphadenitis is less easy in theory than in practice. There are points of similarity between the two diseases, but the experienced clinician is able to diagnose quite a large proportion of cases of mesenteric lymphadenitis with some confidence. Although commonest in children, and more often in young children than infants, no age group is immune. There is often a history of similar previous attacks, and generalized colicky abdominal pain is the most important symptom. This pain is sometimes very severe, and the astute clinician will observe that, although unusually restless during the bouts of pain, the patient may seem quite well between them. Pain is sometimes most marked in the right lower quadrant, but rarely well-defined in position. The bowel habit is generally unaltered, diarrhoea is rare, and nausea and vomiting are variable.

On physical examination the patient with mesenteric adenitis is often less reluctant to move about than one with appendicitis, but this is not a reliable feature. Pyrexia of 101–102° F. (38.3–38.9° C.), or even higher, is quite common and there may be a leucocytosis of 20,000 with 80% neutrophils. Localized tenderness in the right iliac fossa is often rather higher than with appendicitis, and occasionally more widespread if many glands are involved. Sometimes the site of tenderness can be made to shift by turning the patient from the supine to the left lateral position. Rigidity is variable and, on prolonged palpation, frequently becomes less obvious. The rebound sign (Rovsing) may occur with both mesenteric adenitis and appendicitis. Enlarged glands are rarely palpable through the abdominal wall, but gaseous distension of the small gut is not uncommon, and may be a striking feature on plain *x*-ray of the abdomen.

While authorities differ on the question of treatment, if the diagnosis of mesenteric adenitis is certain, and if parental anxiety can be allayed, there is a good case for conservative treatment, as ultimate recovery is the rule. In some cases the diagnosis will be made only at operation, when a normal appendix is removed and the enlarged glands are seen. No harm will have been done and probably no direct good. It is, however, a minority view that removal of the appendix is beneficial to mesenteric lymphadenitis, but in the experience of most clinicians recurrent attacks of pain are not uncommon after operation. If there is any doubt about the diagnosis, especially in a child, it is better to be safe than sorry, and there need be no misgiving about removing a normal appendix. Parents are often unhappy so long as the appendix is still present, and in these circumstances, even if the diagnosis of mesenteric adenitis is certain, it may be best, having explained the probable nature of the trouble and the possibility of recurrent pain, to remove the appendix.

Patch Testing

Q.—*What is the technique of patch testing? Some factory girls who wear rubber gloves to handle a solution of zinc and ammonium chlorides in methylated spirits and water have developed dermatitis of the hands. How would one test the rubber gloves and the solution to see which was responsible? How can one test a volatile substance?*

A.—The patch test is a method of demonstrating epidermal sensitivity. The suspected substance in suitable concentration is placed in contact with the intact skin and held in place with an adhesive dressing for 48 hours. A positive result consists in an eczematous response, usually with vesicles. The positive response is usually present when the dressing is removed after 48 hours, but may be delayed for a few days after this.

A patch test to rubber gloves may be carried out with a piece of rubber about 1 cm. square. This should be placed against the intact skin of the outer part of the arm or the back of the chest; it is then covered with a piece of cellophane a little larger—for example, 2 cm. square. These are then both held in place by a larger piece of adhesive about 5 or 6 cm. square. If a positive result is obtained tests should then be carried out with other samples of rubber in order to determine, if possible, which brand of rubber gloves the girls can wear without trouble.

In the case of the chemical solutions it is important to know their strength. Zinc chloride and ammonium chloride are capable of irritating the normal skin, and patch tests to determine hypersensitivity should be with solutions no stronger than 2%. If the solutions actually in use are stronger than this they are probably primary irritants, and should be diluted if a patch test is made with them. In this case, however, a patch test will be of limited value,

for persons handling a primary irritant are not necessarily hypersensitive if they develop dermatitis. If strong solutions of zinc chloride or ammonium chloride are being handled the diagnosis in these workers should depend mainly upon the observation of the effects of work and vacations, and the fluctuating severity of the eruption.

Volatile substances present considerable difficulty because they tend to evaporate long before sufficient time has elapsed to elicit a reaction. To some extent this may be got over by applying the volatile substance dissolved in oil. The alternative is to occlude the patch completely with an impermeable dressing or even to apply the volatile liquid contained in a small glass cell sealed off with a smear of petroleum jelly. As may well be imagined, this procedure is decidedly awkward, and there is also a likelihood of obtaining a false reaction. A satisfactory technique of testing with volatile substances has not yet been achieved.

Is Primary Tuberculosis Infectious?

Q.—(*a*) *Is primary tuberculosis considered to be infectious? Should a child with primary tuberculosis be admitted to a general paediatric ward? If so, should precautions be taken (masks, gowns, sterilization of crockery and cutlery, etc.)?* (*b*) *What is the point of examining gastric juice in primary tuberculosis? In the vast majority of cases prolonged search reveals no organisms. If an acid-fast bacillus is found, or if an injected guinea-pig dies of tuberculosis, is this considered proof that the patient is infectious to others?*

A.—(*a*) In general, primary tuberculosis in children has probably only a very low degree of infectivity; for practical purposes it may be regarded as non-infectious. During a school epidemic in Denmark Hyge[1] found no case of Mantoux-conversion among the home contacts of a number of children with primary tuberculous lesions, including those with positive gastric lavages. The risks of admitting such a child to a general paediatric ward are in consequence slight. They will obviously be further diminished by the precautions enumerated, though, apart perhaps from the sterilization of crockery, these are probably not worth the trouble involved. None of these remarks apply to cases with progressive parenchymal disease, especially if cavitation is present; such cases should definitely be regarded as infectious.

(*b*) The isolation of tubercle bacilli from gastric juice confirms a diagnosis of tuberculosis, though a negative result in no way excludes it. A positive finding indicates that bacilli are escaping from the respiratory tract, but in any case, as already indicated, the degree of infectivity in most cases is very low. Nowadays drug-sensitivity tests should be carried out on tubercle bacilli isolated from such cases. Owing to the extensive use, and abuse, of chemotherapy in tuberculosis an increasing number of patients are becoming infected with drug-resistant organisms.

Reference

1 *Acta tuberc. scand.*, 1947, **21**, 1.

Dusting Powders for Fleas and Bed Bugs

Q.—*What dusting powders are recommended for travellers to use against bed bugs and fleas? How should they be applied?*

A.—A powder containing pyrethrins for immediate effect plus D.D.T. (dicophane) for residual action would be most satisfactory. If such a combination cannot be purchased, a highly effective insecticide can be produced by mixing a 10% D.D.T. dust with pyrethrum powder containing 0.5% pyrethrins. A 1 to 2-oz. (30 to 60-ml.) bottle of undiluted D.M.P. (dimethyl phthalate) will also prove useful.

Where bed bugs are suspected, a little powder should be shaken into the cracks and crevices of the bed frame and mattress. Since these insects often bite exposed skin, it is as well to protect the face. A few drops of D.M.P. should be rubbed on the hands and thus smeared over the face (avoiding eyelids and lips) just before retiring. Flea bites can be largely prevented by dusting the underwear (or pyjamas) with the insecticide powder. Use about 1 oz. (30 g.) and rub it well in; this should last for a week.

NOTES AND COMMENTS

Faulty Absorption after Partial Gastrectomy.—Mr. J. P. Stephens (Norwich) writes: I was very interested in your answer to the question on faulty absorption after partial gastrectomy ("Any Questions?" *Journal*, September 26, p. 733). These symptoms surely may be explained on a hormonal basis—an important aspect of alimentary physiology which appears to have been neglected. It is generally accepted that patients who have undergone an operation in which the duodenum is closed and a gastro-enterostomy performed do get a true steatorrhoea, as shown by fat balances. They also commonly lose weight, despite an adequate calorie intake. In these operations (which of course exclude a Billroth I) the duodenum is by-passed and no longer are secretogogues passing over it to produce secretin. This hormone is produced in response to the presence of acid meat products, etc., in the duodenum and stimulates the production of pancreatic juice and bile. In its absence, therefore, there will be a partial functional pancreatic insufficiency plus a diminished secretion of bile, so that fat is less emulsified and less split and frank steatorrhoea occurs with loss of weight. There is a physiological gradient down the small bowel in the ability to produce secretin, most being produced in the duodenum, but production gradually ceasing down the jejunum, so that the lower ileum can produce none. It follows, therefore, that the longer the loop of a gastro-enterostomy, and the more efficient a "valve" in preventing afferent loop reflux, the greater will be the steatorrhoea as more secretin-producing bowel is by-passed. In every individual, and in his every mood, the parts played by the hormonal and vagal phases in digestion will vary widely. It follows, therefore, that a patient who digests his food largely via his vagus will have his physiology upset least when the hormonal phase is removed. Conversely, these changes will be greatest in the patient who digests his food mainly via his hormones—probably the type of patient who takes little interest in his food, whose sensations from his eyes, nose, and tongue are suppressed by preoccupying thought from his higher centres. Post-gastrectomy steatorrhoea is not as a rule permanent, presumably because the jejunum increases its ability to produce secretin; and in a Billroth I, where secretogogues with the exception of acid still pass normally over the duodenum, the steatorrhoea will last only until such time as local bruising and oedema have subsided sufficiently to restore its normal function. That the gastric remnant after a Polya or Balfour gastrectomy empties very rapidly is generally accepted, and is borne out by the fact that when a patient vomits bile he often does so immediately following or even during a meal, yet the vomit is as clear as whisky and contains none of the recently ingested food. This rapid emptying of the stomach may be due to the lack of enterogastrone—the hormone normally produced by the stomach in response to fats and which exerts an inhibiting influence over the stomach and upper bowel. If its source has been removed the normal braking mechanism is no longer present and hurry results. The presence or absence of a "shelf" will make little difference, as the width of the stoma is never made smaller than that of the jejunum—the real outlet valve of the stomach. Further investigations along these lines are being undertaken, and it is hoped to publish them shortly.

Our Expert writes: Mr. Stephens's letter refers to various possible hormonal factors to which I deliberately avoided reference. So many explanations of postgastrectomy troubles have been put forward that it was thought best to confine the answer to the particular problem posed by the questioner.

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